THE JOURNAL

CHICAGO, ILLINOIS

VOL. 167, NO. 13 JULY 26, 1958

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FUNCTIONAL APP OACH TO DISABILITY EVALUATION

PRELIMINARY REPORT

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In the evaluation of disabilities the crux of the problem is how to test a person's residual abilities and to record them in clear and consistent form. The procedure here described represents an effort to obtain objective evaluations on a functional basis, broad enough to find universal application, yet detailed enough to permit expansion in any area desired. It takes into account the patient's activities of daily living as well as the results of testing the strength of muscles and the range of joint motion; it also includes psychological, social, and vocational factors. It yields data that can be transferred in extremely compact form to punch cards, convenient for comparing the patient's state at different times, for selecting groups of patients with similar kinds and degrees of disability, for identifying the factors that determine rehabilitation potential, and even for testing the reliability of the evaluation procedure itself. In its definitive form the procedure should be useful to many agencies interested in evaluating a patient's disabilities and the prospects of rehabilitation.

RECENT YEARS have seen an u surge in disability evaluation because of the augmented need created by the ad ances in medicine. The increase of life pan and with it the rise of chronic degenera disease, as well as the high incidence of cripplin cidents, have made the need for a standard thod of evaluating disability paramount.

Recent legislation in the fields of soci security and vocational rehabilitation has forcefu emphasized the lack of a method for determi g a patient's residual ability to function. Althoug in most instances the physician is concerned with e medical impairment alone, as is aptly pointed t in the guide published recently in a suppleme ry edition of The Journal,[1] there are many ca where he is part of a team which must also co der the social, psychological, and vocational fact in determining disability. Furthermore, since e very act of determining disability implies a d sion as to a person's ability or inability to func in all spheres of daily living, a method that co ers the social, psychological, and vocational, as w as the medical factors, would be essential in a tional approach to this problem.

There is no question that a person shou ceive adequate compensation for an injury in ed in the course of his work, but the amount o l disability is not always clear. In a new job tion,

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e worker, although impaired as a result of a previous injury or disease, may not be at all disabled.

The determination of "impairment" is important, as discussed in THE JOURNAL,[1] but disability determination, or the determination of ability to function as a whole person in all spheres of living, is essential for the person's future. The physician plays a key role in this process, for without his findings as to physical function and permissible activity, vocational and other counselors cannot carry out selective placement of the individual.

It has been shown again and again[2] that medical diagnoses are not adequate to evaluate the functional capacities of the disabled. However, there is often a tendency to go to the other extreme and disregard medical diagnosis almost completely in the determination of functional capacity. We feel that because of its prognostic implications the medical diagnosis is essential to this end; our approach is that the medical diagnosis alone is inadequate for the purpose of determining function.

Previous Attempts at Disability Evaluation

In 1950, Spaulding and Erdman[3] pointed out the need for uniform medical evaluation, and as recently as October, 1957, Yamshon[4] indicated that medical evaluation is of itself insufficient to gauge a disabled person's capacities. The crux of the problem, then, is how to test a person's residual abilities and record the results simply, clearly, and in a standard valid manner.

The work of Rinzler, Brown, and Benton[5] in 1951 was an early attempt to evaluate objectively the results of rehabilitation or ability to function. Here a numerical score was given based simply on muscle strength. Weighting of the score by numerous small muscles (as in the hand) was avoided by using areas of the same general muscle size. Range of motion and activities of daily living were observed in the same general terms.

McBride[6] and Hildenbrand[7] are advocates of the method of disability evaluation in which percentage of disability is estimated. McBride considers that factors other than medical, although they impinge on disability determination, are variable, and therefore he uses anatomic and physiological loss as a basis for determination. He employs a formula to calculate the percentage of disability, with values based on estimates of loss percentage in a "unit of functional deficiency," taking job requirements into account, and a "unit of physical disorders."

The Canadian Army[8] and the U. S. Army[9] have also seen the need for developing disability profiles. In 1943, the Canadian Army published the second edition of "Physical Standards and Instructions for the Medical Examination of Serving Soldiers and Recruits." This contains a disability evaluation system known as "PULHEMS Profile," where P = physique, U = upper extremity, L = lower extremity, H = hearing and ears, E = eyes and vision, M = mental capacity, and S = stability (emotional). Each of these is rated 1 through 5, where 1 is normal and 5 is totally unfit. This system is now being revised and tested and is known as "PLUMSHEAF." In the U. S. Army, the system is known as "PULHES" and the numerical ratings are 1 through 4. "S" takes the place of both "M" and "S" in the Canadian system, and stands for "psychiatric." Prognosis is also considered and "R" (remediable), "T" (temporary), or "D" (permanently disqualifying for overseas service) may be added to the rating. Moskowitz[2c] has also revised this system for use in evaluating the group of persons chronically ill and aging.

The question of function in activities of daily living has been answered by the work of many people, such as Brown[10] and Lawton,[11] and Hoberman and associates.[12] Brown has compiled a list of 100 items of daily activity which are timed and scored. The score is the simple addition of activities performed. As other activities are learned, the score increases. This author has also compiled a prevocational motor skill inventory for cerebral palsied children in which the type of activity (e. g., sewing) is matched against a related occupation (e. g., seamstress). There are 100 items, with a one-point score for each item. Lawton has compiled a test list of daily living activities in all phases, including consideration of the home situation. This is an important step forward, since function in a special setting such as a hospital or rehabilitation center is not necessarily carried over to the home and job situations. The use of such forms as these is now widespread and practically standard.

Recent work has been carried out at the New York University–Bellevue Medical Center to attempt to obtain objective evaluations of disability on a functional basis. In one such study an attempt has been made to include the various areas important in the evaluation and rehabilitation of the homebound (physical, psychological, social, and vocational). However, in that study, as in most of the work done to date, the field covered is narrow—either because the tests cover only one or two of the areas mentioned above or because the tests were designed for a specific type of patient or disability.

Disability Evaluation Forms

In the project under discussion, we have attempted to create an instrument for disability evaluation which would be broad enough to find universal application and at the same time would permit detailed expansion in any area desired. The forms are made to fit into the 80 columns of an I. B. M. card with room for 12 items in each column (X, Y, 0, 1, 2, 3, 4, 5, 6, 7, 8, 9) (see table). Th[illegible] oad data, which we feel would apply to the

*Disability Evaluation Project: New York University—Bellevue Medical Center Institute of Physical Medicine and Rehabilitation**

Patient's Name .... State .... Institution ....

6 7 8 9 10 11 12 13 14 15 16 17 18
PATIENT'S INSTITUTION NUMBER ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ DATE Month ☐ Year 19 ☐ ☐ AGE ☐

19. SEX male ☐x female ☐y RACE________________ PHYSICAL STATUS Hypermorph ☐7 Mesomorph ☐8 Hypomorph ☐9

STATEMENT OF DISABILITY

20. Pain moderate ...... ☐x
Pain severe .... ☐y

Etiologies of Principal Disabilities

Infection .... ☐0
Non-specific inflammation .... ☐1
Congenital .... ☐2
Degenerative .... ☐3
Traumatic .... ☐4
Vascular .... ☐5
Toxic .... ☐6
Metabolic .... ☐7
Allergic .... ☐8
Tumor .... ☐9

21. ORGAN SYSTEM Disease
Cardiovascular Disease .... ☐x
Neurological Disease . ☐y
Respiratory Disease .. ☐0
Gastro-Intestinal Disease .... ☐1
Musculoskeletal Disease .... ☐2
Genito-Urinary Disease .... ☐3
Metabolic or Allergic .... ☐4

Degree of Independence

Bedridden .... ☐5
Wheelchair with Assistance .... ☐6
Wheelchair Independent .... ☐7
Ambulatory .... ☐8
Able to Travel .... ☐9

22. PSYCHIATRIC
Motivation Good ... ☐x
Poor ... ☐y

SOCIAL

Living Arrangements
Home or Room ..... ☐0
Institution .... ☐1

Financial Resources
Adequate .... ☐2
Inadequate .... ☐3

VOCATIONAL

Employable .... ☐4
Not Employable ...... ☐5
Employable with reservations .... ☐6

REHABILITATION POTENTIAL

Good .... ☐7
Poor .... ☐8
Undetermined .... ☐9

23. % Value.
Primary diagnosis is the one that is the most important factor in the disability, and the secondary diagnosis is the one that is the next most important factor in the disability. Diagnoses are to be coded in six digits for each diagnosis, according to the "Standard Nomenclature of Disease and Operations."

24 25 26 27 28 29
PRIMARY DIAGNOSIS ☐ ☐ ☐ ☐ ☐ ☐

30 31 32 33 34 35
SECONDARY DIAGNOSIS ☐ ☐ ☐ ☐ ☐ ☐

INTERNAL MEDICINE

36. CARDIAC
Etiology
Hypertensive and arteriosclerotic ..... ☐x
Rheumatic .... ☐y
Other .... ☐0

Functional Classification
I. ☐1
II. ☐2
III. ☐3
IV. ☐4

Therapeutic Classification
A. ☐5
B. ☐6
C. ☐7
D. ☐8
E. ☐9

37. VASCULAR
Localization
Coronary .... ☐x
Cerebral .... ☐y
Peripheral .... ☐0
Thrombosis .... ☐1
Embolism .... ☐2
Rupture .... ☐3
Gangrene .... ☐4
Arteriosclerosis ...... ☐5
Hypertension .... ☐6
Endarteritis (Buerger's etc.) .... ☐7
Thrombophlebitis .... ☐8
Other (aneurism, disseminated arterial disease, viz. lupus, polyarteritis, etc.) .... ☐9

38. PULMONARY
Tuberculosis .... ☐x
Pneumonia (all types) .... ☐y
Pleurisy .... ☐0
Chronic Bronchitis ... ☐1
Bronchiectasis .... ☐2
Emphysema .... ☐3
Fibrosis .... ☐4
Abscess .... ☐5
Mycotic Diseases ..... ☐6
Embolism .... ☐7
Tumor .... ☐8
Other .... ☐9

39. GASTROINTESTINAL
Localization
Esophagus, Stomach, Duodenum .... ☐x
Small Intestine and Peritoneum .... ☐y
Large Intestine and Rectum .... ☐0
Liver, Gall Bladder, Pancreas .... ☐1

Pathology

Tumor .... ☐2
Tuberculosis .... ☐3
Infection .... ☐4
Non-specific inflammation .... ☐5
Obstruction .... ☐6
Ulcer with or without complications ...... ☐7
Cirrhosis with or without complications ...... ☐8
Calculus .... ☐9

40. ENDOCRINE
Pituitary Anterior ... ☐x
Pituitary Posterior .. ☐y
Thyroid .... ☐0
Parathyroid .... ☐1
Adrenal Cortex ...... ☐2
Testes or Ovaries .... ☐3
Hyperfunction .... ☐4
Hypofunction .... ☐5
Infection (including T. B.) ... ☐6
Nonspecific inflammation .... ☐7
Congenital and degenerative .... ☐8
Tumor .... ☐9

41. Allergic
Hay fever .... ☐x
Bronchial Asthma ... ☐y
Other .... ☐0

Metabolic
Diabetes mellitus . .. ☐1
Endocrine Obesity ... ☐2

Nutritional
Avitaminosis ...... B. ☐3
C. ☐4
D. ☐5
Sprue .... ☐6
Malnutrition .... ☐7

42. BLOOD DISEASES
Hyperchromic (inc. Pernicious) ... ☐x
Deficiency inc. post-hemorrhagic .. ☐y
Aplastic .... ☐0

Anemia
Sickle-cell .... ☐1
Splenic (Banti's) .... ☐2
Hemolytic .... ☐3
Polycythemia .... ☐4
Leukemia (myeloid and lymphatic, acute) .. ☐5
Leukemia (myeloid and lymphatic, chronic) .... ☐6
Hemophilia .... ☐7
Hodgkin's Disease ... ☐8
Purpura .... ☐9

43. POISONING, DISEASES DUE TO PHYSICAL AGENTS, MISCELLANEOUS
Alcoholism .... ☐x
Drug addiction ...... ☐y
Heavy metal poisoning .... ☐0
Carbon monoxide poisoning .... ☐1
Other poisoning ..... ☐2
Heat exhaustion .... ☐3
Heat stroke .... ☐4
Burns .... ☐5
Trauma (dislocation without fracture, lacerations, etc.) ... ☐6
Mental, Psychoneurotic, and Personality disorders .... ☐7
Tumors of Reticulo-endothelial System . ☐8
Tumors not covered elsewhere .... ☐9

4. SKIN
Infection
Bacterial .... ☐x
Fungal .... ☐y
Metazoan (scabes, lice) .... ☐0
Possibly infectious (Pemphigus, Dermatitis Herpetiformis) .... ☐1
Acne (Vulgaris or Rosacea) .... ☐2
Allergy .... ☐3
Psoriasis .... ☐4
Lupus (circumscribed or disseminated) Erythematosus .... ☐5
Scleroderma .... ☐6
Tumor or precancerous diseases .... ☐7
Decubitus Ulcers ..... ☐8
Other .... ☐9

5. GENERAL PHYSICAL STATUS (Marked Obesity≈25% or more over normal weight)
Simple (exogenous) Obesity
Moderate .... ☐x
Marked .... ☐y
Well Developed, well nourished .... ☐0
Cachexia (Nutritional or Metabolic .... ☐1
Cardiac Neurosis and Neurocirculatory Asthenia .... ☐2
Migraine .... ☐3
Tension or other severe recurrent headache . ☐4
Poor Dental Condition .... ☐5
Focal Infection ...... ☐6
Chronic Constipation ...... ☐7
Other .... ☐8

6. % Value.

*Disability Evaluation Project: New York University–Bellevue Medical Center Institute of Physical Medicine and Rehabilitation**

SPECIAL SENSES

47. HEARING

Deafness
- Unilateral, partial ... ☐x
- Unilateral, complete . ☐y
- Bilateral, partial .... ☐0
- One partial, one complete .... ☐1
- Bilateral, complete ... ☐2
- Can be improved with hearing aid .... ☐3

SPEECH

Aphasia
- Expressive .... ☐4
- Receptive .... ☐5
- Global .... ☐6
- Stuttering (Functional) .... ☐7
- Peripheral speech difficulty .... ☐8
- Diseases of ear (inc. tumor, labyrinthitis, etc.) .... ☐9

48. EYE
- Partial or complete blindness, unilateral ☐x
- Uncorrectable bilateral, severely decreased visual acuity .... ☐y
- One complete blindness, one uncorrectable severely dec. vis. acuity .... ☐0
- Legal blindness (bilateral) .... ☐1
- Complete blindness (bilateral) .... ☐2
- Cataract .... ☐3
- Glaucoma, primary or secondary .... ☐4
- Corneal Opacity ...... ☐5
- Arteriosclerotic, Hypertensive, & Diabetic Retinopathy .... ☐6
- Primary Optic Atrophy .... ☐7
- Infection .... ☐8
- Tumor .... ☐9

49. % Value.

GENITO URINARY SYSTEM

50. KIDNEY & BLADDER
- Renal Insufficiency and Uremia .... ☐x
- Calculus, Renal ...... ☐y
- Calculus, Bladder ... ☐0
- Infection including T. B. .... ☐1
- Glomerulonephritis .. ☐2
- Nephrosis .... ☐3
- Hypertensive Renal Disease .... ☐4
- Hydronephrosis ...... ☐5
- Congenital Conditions .... ☐6
- Tumor .... ☐7
- Incontinence .... ☐8
- Trauma .... ☐9

51. GENITAL SYSTEM

Male — Localization
- Scrotum .... ☐x
- Testis .... ☐y
- Epididymis .... ☐0
- Spermatic Cord ...... ☐1
- Seminal Vesicles ...... ☐2
- Prostate .... ☐3
- Penis .... ☐4
- Tumor .... ☐5
- Infection including T. B. .... ☐6
- Congenital Conditions .... ☐7
- Benign Prostatic Hypertrophy .... ☐8
- Trauma .... ☐9

Female — Localization
- Vulva .... ☐x
- Vagina .... ☐y
- Cervix and Uterus ... ☐0
- Tubes .... ☐1
- Ovary .... ☐2
- Breast .... ☐3
- Benign Tumor, including fibroid .... ☐4
- Malignant Tumor .... ☐5
- Infection including T. B. .... ☐6
- Congenital Conditions .... ☐7
- Severe Dysmenorrhea ☐8
- Trauma (including residual of injury during delivery) .... ☐9

52. % Value.

NEUROMUSCULOSKELETAL

53. ETIOLOGY
- Effects of specific Infection .... ☐x
- Nonspecific Inflammatory Diseases (e. g. Collagen Disease) .... ☐y
- Degenerative .... ☐0
- Traumatic .... ☐1
- Vasculär .... ☐2
- Toxic .... ☐3
- Tumor .... ☐4
- Allergy .... ☐5
- Metabolic (Glandular) .... ☐6
- Nutritional Deficiency (i. e. Neuritis) ...... ☐7
- Congenital and Birth Injury .... ☐8

54. LOCALIZATION
- Cerebral .... ☐x
- Cerebellar .... ☐y
- Midbrain and Brain Stem .... ☐0

Motor Nervous System Defect
- Spinal .... ☐1
- Peripheral Nerve ..... ☐2
- Motor End Plate ..... ☐3

Musculoskeletal Defect
- Muscle and Tendon .. ☐4
- Joint .... ☐5
- Bone .... ☐6

Sensory Defect (Below Lesion)
- Intact .... ☐7
- Partial Loss .... ☐8
- Complete Loss .... ☐9

55. SPECIAL AND COMMON CONDITIONS
- Monoplegia Upper Extremity .... ☐x
- Monoplegia Lower Extremity .... ☐y
- Hemiplegia .... ☐0
- Paraplegia .... ☐1
- Quadriplegia .... ☐2
- Skull Fracture .... ☐3

Fracture (including 2° Fracture)
- Hip Fracture .... ☐4
- Spine Fracture .... ☐5
- Other Fractures ...... ☐6
- Amputee (detail in ADL) .... ☐7
- Osteomyelitis .... ☐8
- Hernia .... ☐9

SPECIAL AND COMMON CONDITIONS

Arthritis
- Rheumatoid Arthritis and Spondylitis .... ☐x
- Traumatic .... ☐y
- Osteoarthritis .... ☐0
- Gout .... ☐1
- Psychogenic and Miscellaneous ...... ☐2
- Parkinson's Disease .. ☐3
- Poliomyelitis .... ☐4
- Multiple Sclerosis .... ☐5
- Epilepsy .... ☐6
- Cerebral Palsy .... ☐7
- Muscular Dystrophy .. ☐8
- Sciatica .... ☐9

MUSCLE TEST

Note: (a) If "Equal" is punched, then Major Side is right side.

Note: (b) Major Side = Major Lesion (to avoid confusion).

N. & G. equals Normal and Good

57. MAJOR SIDE

Major Side
- Left ... ☐x
- Right .. ☐y
- Equal .. ☐0

Upper Extremity
- N. & G. .... ☐1
- Fair .... ☐2
- Below Fair .... ☐3

Lower Extremity
- N. & G. .... ☐4
- Fair .... ☐5
- Below Fair .... ☐6

Neck
- N. & G. .... ☐7
- Fair .... ☐8
- Below Fair .... ☐9

58. MINOR SIDE

Upper Extremity
- N. & G. .... ☐1
- Fair .... ☐2
- Below Fair .... ☐3

Lower Extremity
- N. & G. .... ☐4
- Fair .... ☐5
- Below Fair .... ☐6

Trunk
- N. & G. .... ☐7
- Fair .... ☐8
- Below Fair .... ☐9

RANGE OF MOTION

Note: (a) If "Equal" is punched, then Major Side is right side.

Note: (b) Major Side = Major Lesion (to avoid confusion).

59. MAJOR SIDE

Major side
- Left ... ☐x
- Right .. ☐y
- Equal .. ☐0

Upper Extremity
- Complete .... ☐1
- Partial .... ☐2
- None .... ☐3

Lower Extremity
- Complete .... ☐4
- Partial .... ☐5
- None .... ☐6

Neck
- Complete .... ☐7
- Partial .... ☐8
- None .... ☐9

60. MINOR SIDE

Upper Extremity
- Complete .... ☐1
- Partial .... ☐2
- None .... ☐3

Lower Extremity
- Complete .... ☐4
- Partial .... ☐5
- None .... ☐6

Trunk
- Complete .... ☐7
- Partial .... ☐8
- None .... ☐9

Footnote: Complete means complete or major part of range of motion is present for the whole limb. Partial means less than the major part of range of motion is present for the whole limb. None means no range of motion is present.

61. % Value.

*Disability Evaluation Project. New York University—Bellevue Medical Center Institute of Physical Medicine and Rehabilitation**

ACTIVITIES OF DAILY LIVING TEST

62 COMMUNICATION
Writing
Complete ☐ x
Partial ☐ y
None ☐ 0

Speech
Complete ☐ 1
Partial ☐ 2
None ☐ 3

LEVEL AMBULATION
Complete ☐ 4
Partial ☐ 5
None ☐ 6

WHEELCHAIR ACTIVITIES (Where wheelchair is used)
Complete ☐ 7
Partial ☐ 8
None ☐ 9

63 Bed Activities
Complete ☐ x
Partial ☐ y
None ☐ 0

Personal Hygiene
Complete ☐ 1
Partial ☐ 2
None ☐ 3

Dressing
Complete ☐ 4
Partial ☐ 5
None ☐ 6

Eating
Complete ☐ 7
Partial ☐ 8
None ☐ 9

64 ELEVATION
Stairs & Curb
Complete ☐ x
Partial ☐ y
None ☐ 0

TRAVEL (Important for Vocational Reasons)

Car
Complete ☐ 1
Partial ☐ 2
None ☐ 3

Subway
Complete ☐ 4
Partial ☐ 5
None ☐ 6

Bus
Complete ☐ 7
Partial ☐ 8
None ☐ 9

65 APPLIANCE USED
Major ☐ x
Minor ☐ y
Both ☐ 0

Leg Brace ☐ 1
Spinal Brace ☐ 2
Crutches ☐ 3
Cane ☐ 4

Prosthesis
Major B K or B E ☐ 5
Major A K or A E ☐ 6
Minor B K or B E ☐ 7
Minor A K or A E ☐ 8

FOOTNOTE 1) Wheel chair omitted in Col 65 since it is picked up in detail card in A D L
2) Complete means the activity can be performed completely without assistance Partial means the activity can be performed only with assistance in part of the activity None means the patient is unable to perform any part of the activity without assistance

66 % Value

SOCIOECONOMIC

67 ECONOMIC RESOURCES
Fully Employed ☐ 1
Partially Employed ☐ 2

Family Support ☐ 3
V A Pension ☐ 4

OASI Pension ☐ 5
Compensation ☐ 6

Individual Annuity ☐ 7
Other Resources ☐ 8

No Resources ☐ 9

68 HOUSING
Adequate ☐ x
Inadequate ☐ y

TYPE OF HOUSING
Private Home ☐ 0
Apartment ☐ 1
Rented Room ☐ 2

Boarding Home ☐ 3
Institution, nonhospital ☐ 4
Hospital ☐ 5

Nursing Home ☐ 6
Homeless ☐ 7

Ground Floor or Elevator ☐ 8
Stair Climbing Required ☐ 9

69 FAMILY UNIT LIVED WITH
Alone ☐ 1
Spouse ☐ 2

Spouse & Dependent Children ☐ 3
Dependent Children ☐ 4

With Adult Children ☐ 5
Supporting Parent(s) ☐ 6

Dependent Parent(s) ☐ 7
Other Relatives ☐ 8

Other Living Arrangements ☐ 9

70 % Value

PSYCHIATRIC

71 Organic Brain Syndrome (Congenital or Acquired) ☐ x
Functional Psychosis ☐ y

Psychoneurosis ☐ 0
Memory Loss ☐ 1
Disorientation ☐ 2

ASPIRATIONS
Realistic ☐ 3
Unrealistic ☐ 4

I Q
Below Average ☐ 5
Average ☐ 6
Above Average ☐ 7

ABILITY TO LEARN
Poor ☐ 8
Good ☐ 9

72 % Value

VOCATIONAL

73 EDUCATION
Scholastic Record
Good ☐ x
Fair ☐ y
Poor ☐ 0

Below School Age ☐ 1
Still attending School ☐ 2
Grade School Partial ☐ 3

Grade School Completed ☐ 4
Technical School Completed ☐ 5
High School Completed ☐ 6

College Completed ☐ 7
Professional School Completed ☐ 8
None ☐ 9

74 EMPLOYMENT STATUS AT EVALUATION
Level of Employment
Skilled (Professional) ☐ x
Semiskilled ☐ y
Unskilled ☐ 0

Housewife ☐ 1
Fully Employable ☐ 2

Partially Employable ☐ 3
Employable at home only ☐ 4

Unemployable ☐ 5
Retired ☐ 6

School or preschool ☐ 7

75 % Value

REHABILITATION POTENTIAL

76 MEDICAL PROGNOSIS
Time of Evaluation
Initial Medical Exam ☐ x
Pre Rehabilitation ☐ y
Post Rehabilitation ☐ 0

Cure ☐ 1
Improvement with return to full activity ☐ 2
Improvement with return to slightly limited activity ☐ 3

Improvement with return to markedly limited activity ☐ 4
Improvement with return to self-care only ☐ 5

No significant improvement anticipated ☐ 6
Recurrent progressive deterioration ☐ 7

Slow progressive deterioration ☐ 8
Rapid deterioration or demise ☐ 9

77 ESTIMATED MAXIMUM LENGTH OF TIME FOR REHABILITATION
None ☐ x
Up to 30 days ☐ y
31 to 60 days ☐ 0

2 to 3 months ☐ 1
3 to 4 months ☐ 2
4 to 6 months ☐ 3

6 to 9 months ☐ 4
9 to 12 months ☐ 5

12 to 18 months ☐ 6
18 to 24 months ☐ 7

Over 24 months ☐ 8
Undeterminable ☐ 9

78 DEGREE OF INDEPENDENCE (ESTIMATED)
Self Care
Complete ☐ x
Partial (with assistance) ☐ y
None ☐ 0

Ambulation
Full ☐ 1
Limited ☐ 2
No ☐ 3

Wheelchair
Independent ☐ 4
Nonindependent ☐ 5
Bedfast ☐ 6

Travel
Auto self-driven ☐ 7
Auto as passenger ☐ 8
Public transportation ☐ 9

79 FUTURE EMPLOYMENT AND LIVING STATUS
Potential Disposition
Home & Family ☐ x
Room alone ☐ y
Institution ☐ 0

Employable at former Occupation ☐ 1
Partially employable at former Occupation ☐ 2

Definitely Employable at another Occupation only ☐ 3
Partially employable at former Occupation but fully employable at another Occupation ☐ 4

Employable at home only ☐ 5
Housewife ☐ 6

Unemployable or retired ☐ 7
School or Pre-school ☐ 8
Undeterminable ☐ 9

80 % Value.

Disability Evaluation Project: New York University–Bellevue Medical Center Institute of Physical Medicine and Rehabilitation[*]

MUSCLE TEST—DETAIL CARD
LEFT SIDE

36. Neck flexors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Neck extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Trunk flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Trunk extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

37. Trunk rotators
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Trunk elevators
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Hip flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Hip extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

38. Hip abductors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Hip adductors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Hip external rotators
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Hip internal rotators
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

39. Knee flexors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Knee extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Ankle flexors (plantar)
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Ankle extensors (dorsi)
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

40. Foot eversion
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Foot inversion
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Toe flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Toe extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

41. Scapular abductors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Scapular adductors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Scapular elevators
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Scapular depressors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

42. Shoulder flexors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Shoulder extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Shoulder abductors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Shoulder adductors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

43. Shoulder external rotators
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Shoulder internal rotators
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Elbow flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Elbow extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

44. Forearm supinators
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Forearm pronators
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Wrist flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Wrist extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

45. Wrist radial duction
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Wrist ulnar duction
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Finger flexors (forearm)
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Finger extensors (forearm)
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

46. Finger intrinsics
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Thumb opposition
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Thumb intrinsics
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Thumb (forearm muscles): Abductor Pollicis longus, flexor pollicis longus, extensor pollicis longus
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

RIGHT SIDE

47. Neck flexors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Neck extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Trunk flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Trunk extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

48. Trunk rotators
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Trunk elevators
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Hip flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Hip extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

49. Hip abductors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Hip adductors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Hip external rotators
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Hip internal rotators
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

50. Knee flexors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Knee extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Ankle flexors (plantar)
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Ankle extensors (dorsi)
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

51. Foot eversion
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Foot inversion
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Toe flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Toe extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

52. Scapular abductors
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Scapular adductors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Scapular elevators
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Scapular depressors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

53. Shoulder flexors
Good and Normal,...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Shoulder extensors
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Shoulder abductors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Shoulder adductors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

54. Shoulder external rotators
Good and Normal ...... ☐x
Fair .... ☐y
Below Fair .... ☐0

Shoulder internal rotators
Good and Normal ...... ☐1
Fair .... ☐2
Below Fair .... ☐3

Elbow flexors
Good and Normal ...... ☐4
Fair .... ☐5
Below Fair .... ☐6

Elbow extensors
Good and Normal ..... ☐7
Fair .... ☐8
Below Fair .... ☐9

*Disability Evaluation Project: New York University—Bellevue Medical Center Institute of Physical Medicine and Rehabilitation**

55. Forearm supinators
Good and Normal ...... ☐x
Fair ...... ☐y
Below Fair ...... ☐0

Forearm pronators
Good and Normal ...... ☐1
Fair ...... ☐2
Below Fair ...... ☐3

Wrist flexors
Good and Normal ...... ☐4
Fair ...... ☐5
Below Fair ...... ☐6

Wrist extensors
Good and Normal ...... ☐7
Fair ...... ☐8
Below Fair ...... ☐9

56. Wrist radial duction
Good and Normal ...... ☐x
Fair ...... ☐y
Below Fair ...... ☐0

Wrist ulnar duction
Good and Normal ...... ☐1
Fair ...... ☐2
Below Fair ...... ☐3

Finger flexors (forearm)
Good and Normal ...... ☐4
Fair ...... ☐5
Below Fair ...... ☐6

Finger extensors (forearm)
Good and Normal ...... ☐7
Fair ...... ☐8
Below Fair ...... ☐9

57. Finger intrinsics
Good and Normal ...... ☐x
Fair ...... ☐y
Below Fair ...... ☐0

Thumb opposition
Good and Normal ...... ☐1
Fair ...... ☐2
Below Fair ...... ☐3

Thumb intrinsics
Good and Normal ...... ☐4
Fair ...... ☐5
Below Fair ...... ☐6

Thumb (forearm muscles): Abductor pollicis longus, flexor pollicis longus, extensor pollicis longus
Good and Normal ...... ☐7
Fair ...... ☐8
Below Fair ...... ☐9

58. % Value.

RANGE OF MOTION — DETAIL CARD†

Full=Full and Major part of ROM. Partial=Less than Major part of ROM. None=No ROM is present.

LEFT SIDE

59. Shoulder flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Shoulder extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Shoulder abduction
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Shoulder adduction
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

60. Shoulder external rotation
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Shoulder internal rotation
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Elbow flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Elbow extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

61. Radioulnar supination
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Radioulnar pronation
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Wrist extension
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Wrist flexion
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

62. Wrist radial duction
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Wrist ulnar duction
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

M. P. flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

M. P. extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

63. I.P. (proximal) flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

I.P. (proximal) extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

I.P. (distal) flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

I.P. (distal) extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

64. Thumb M.P. flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Thumb M.P. extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Thumb I.P. flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Thumb I.P. extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

65. Hip flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Hip extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Hip adduction
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Hip abduction
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

66. Hip external rotation
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Hip internal rotation
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Knee flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Knee extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

67. Ankle flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Ankle extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Foot eversion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Foot inversion
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

68. Toe M.P. flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Toe M.P. extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Toe I.P. flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Toe I.P. extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

RIGHT SIDE

69. Shoulder flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Shoulder extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Shoulder abduction
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Shoulder adduction
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

70. Shoulder external rotation
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Shoulder internal rotation
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Elbow flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Elbow extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

71. Radioulnar supination
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Radioulnar pronation
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Wrist extension
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Wrist flexion
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

72. Wrist radial duction
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Wrist ulnar duction
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

M. P. flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

M. P. extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

73. I.P. (proximal) flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

I.P. (proximal) extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

I.P. (distal) flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

I.P. (distal) extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

74. Thumb M.P. flexion
Full ...... ☐x
Partial ...... ☐y
None ...... ☐0

Thumb M.P. extension
Full ...... ☐1
Partial ...... ☐2
None ...... ☐3

Thumb I.P. flexion
Full ...... ☐4
Partial ...... ☐5
None ...... ☐6

Thumb I.P. extension
Full ...... ☐7
Partial ...... ☐8
None ...... ☐9

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EFFECT OF METHOXSALEN ON LIVER FUNCTION

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Four liver function tests were performed serially in 24 normal human subjects before, during, and after administration of 30 mg. of methoxsalen (8-methoxypsoralen) along with casual exposure to ultraviolet irradiation to 12 of the subjects, the remaining 12 subjects receiving placebos. In the group receiving methoxsalen, two subjects noted a slight increase in beard hair growth, and one reported "peptic ulcer" symptoms, which disappeared as the therapy was continued. Although a selected profile of liver function tests and blood constituents relating to liver function were within normal limits throughout the course of administration of methoxsalen, it cannot yet be concluded that the drug is safe for the general population.

One of the furocoumarins, methoxsalen (8-methoxypsoralen), is being used in conjunction with ultraviolet irradiation in the United States, Europe, and the Middle East for the treatment of vitiligo.[1] The possible widespread use of this drug in selected patients for increasing tolerance to solar radiation [2] has prompted us to investigate its effect on liver function.

During the early period of investigation of the effect of orally administered methoxsalen and ultraviolet light on the course of vitiligo, Lerner and coworkers [1d] reported results of the cephalin-cholesterol flocculation test (Hanger's test) in 11 patients receiving daily doses of 10 to 30 mg. of the drug. the 11 patients, 7 were reported to show "quesable changes" in the cephalin-cholesterol floclation test after receiving the drug for one to ee months. "In five cases, only the 48-hour tests ere positive; in the other two, one was 1+ and the other 2+ at 24 hours." On the basis of these findings Lerner and associates suggested that cephalin-cholesterol flocculation tests should be performed for three months. In the subsequent four years since this report appeared, there have been sporadic unpublished reports of abnormal liver function findings in patients taking methoxsalen for the treatment of vitiligo. Elliott,[1e] in a study of the treatment of 22 patients with vitiligo, observed elevated findings in the sulfobromophthalein test in two patients. Unfortunately, the pretreatment sulfobromophthalein tests were not reported, and it is not possible to interpret the elevated results in these two patients. It is possible that either or both of these patients may have had subclinical viral hepatitis or infectious mononucleosis or that the elevated results were related to the methoxsalen therapy.

In the present study, four hepatic function tests have been performed serially during a three-month period in 12 normal male subjects receiving daily doses of 30 mg. of methoxsalen and in 12 comparable male subjects receiving a placebo. Subjects in both groups had only casual exposure to sunlight, and, hence, this trial does not relate to the possible effects on the liver of products of the interaction of methoxsalen with ultraviolet irradiation.

Methods

Laboratory evaluation of liver function was based on the thymol turbidity reaction of the serum, the zinc turbidity reaction, cephalin-cholesterol flocculation, and sulfobromophthalein excretion. All procedures were done by the staff of the metabo-

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From the divisions of dermatology and metabolism, University of Oregon Medical School.

lism research laboratory at the University of Oregon Medical School Hospital. Normal limits have been previously described by this laboratory in its "Handbook of Standards." These procedures were selected from a large number of tests performed by this laboratory, since they offer broad scanning in addition to certain individual advantages. The thymol and zinc turbidity reactions, which are indications of impaired liver function over a broad range of liver injury of unrelated etiology, are not tests of liver function and are not valuable for screening purposes but are best suited to measuring the degree of damage. Cephalin-cholesterol flocculation tests, however, are considered excellent screening procedures, especially for bringing out early changes or subclinical impairment of liver function. The sulfobromophthalein test is the most sensitive screening test available and is confirmatory when the more gross tests that simply indicate disturbed liver function are either minimally disturbed or completely negative.

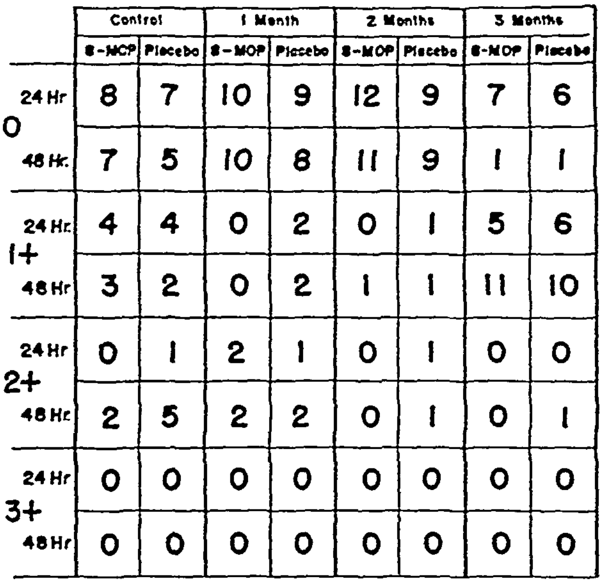
The thymol turbidity test was performed by a modified method for the quantitative determination of thymol turbidity reaction of serum. The upper limit of normal was taken to be four units.[3] The zinc turbidity reaction was determined by the method of Kunkel and associates.[4] The upper limit of normal was taken to be 12.5 units. Cephalin-cholesterol flocculation was tested by the method of Hanger,[5] as directed by the Wilson Laboratories. Readings were taken at 24 and 48 hours, with a 2+ reading in 24 hours as the upper limit of normal.

Sulfobromophthalein retention was determined spectrophotometrically on serum drawn 45 minutes after injection of 5 mg. of dye per kilogram of body weight.[6] The upper limit of normal was taken to be 4% retention in 45 minutes. Blood samples for the liver function tests were all drawn with the subject in fasting state.

Twenty-five male medical students were selected as subjects for the study. All were in good physical condition, and none had a history of liver disease or clinical jaundice. One subject was eliminated from the study after one month because his cephalin-cholesterol flocculation test was 4+ in 24 hours in the control period (before ingestion of the drug). The test results for this subject are not included in the analysis.

Twelve subjects were selected by random numbers from the group and given 30 mg. of methoxsalen each day for three months. This dosage is slightly higher than the daily dose given to patients (10 to 20 mg.). The subjects took the total amount once daily and were monitored by having to fill in a chart each day indicating that the drug had been taken. The 12 subjects not receiving the drug were given a placebo (identical capsule). A "double-blind" experiment design was used. Control tests were completed before any drug was administered. Subsequent tests were made at the end of each of the three months.

Subjects 1-12 (six on placebo and six on methoxsalen therapy) received the drug during the months of November, December, and January and hence were not exposed to much sunlight in Oregon. Subjects 13-25 (six on placebo and seven on active methoxsalen therapy) received the drug during the months of March, April, and May and were exposed to varying amounts of sunlight. Six of the seven subjects who received the methoxsalen during the spring months reported augmentation of their response to sunlight. None of the six subjects taking the placebo noticed any difference in their erythema or pigment response. This is a significant difference between groups with 99% confidence limits by the Chi-square test.



		Control		1 Month		2 Months		3 Months	
		8-MOP	Placebo	8-MOP	Placebo	8-MOP	Placebo	8-MOP	Placebo
0	24 Hr	8	7	10	9	12	9	7	6
	48 Hr	7	5	10	8	11	9	1	1
1+	24 Hr	4	4	0	2	0	1	5	6
	48 Hr	3	2	0	2	1	1	11	10
2+	24 Hr	0	1	2	1	0	1	0	0
	48 Hr	2	5	2	2	0	1	0	1
3+	24 Hr	0	0	0	0	0	0	0	0
	48 Hr	0	0	0	0	0	0	0	0

Fig. 1.—Results of cephalin-cholesterol flocculation test performed at monthly intervals to compare 12 subjects taking placebo with 12 taking 30 mg. of methoxsalen (8-MOP) per day.

Results

The results of the cephalin-cholesterol flocculation tests are presented in figure 1. Although a minor month-to-month variation is apparent, the placebo and the methoxsalen groups are similar. The means and ranges of the other liver function tests are presented in figures 2, 3, and 4. A close similarity is noted in the groups. There is no significant difference in the hepatic function tests of the subjects receiving methoxsalen when compared with the subjects receiving the placebo. No subject showed any abnormal results in the tests indicative of liver function impairment at any time during the treatment period.

Additional but uncontrolled evidence is available from liver function tests we have done in the past five years in patients taking methoxsalen plus receiving ultraviolet irradiation for the treatment of vitiligo. Thirty-eight patients have received daily doses of 15 to 60 mg. over a period of 3 to 36 months. The results of cephalin-cholesterol flocculation tests performed in these patients were all within normal limits. In five patients the thymol turbidity reaction was determined in addition to the cephalin-cholesterol flocculation test, and these results were within normal limits. Caution must be used in evaluating liver function by the latter test alone. It is not specific and frequently yields false-positive results. The cephalin-cholesterol flocculation test is helpful if used in conjunction with other liver function tests.

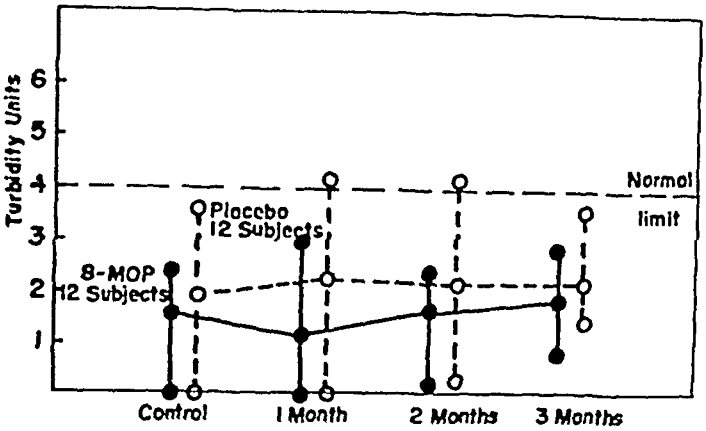


Fig. 2.—Means and extremes of thymol turbidity reactions determined at monthly intervals to compare 12 subjects taking placebo with 12 taking 30 mg. of methoxsalen (8-MOP) per day.

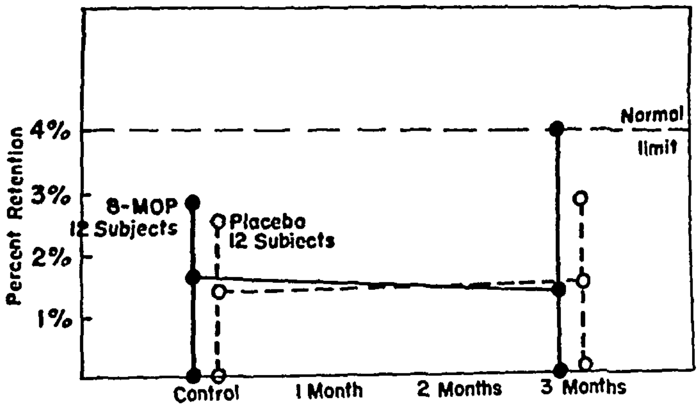


Fig. 3.—Means and extremes of sulfobromophthalein retentions determined before and after ingestion of drug to compare 12 subjects taking placebo with 12 taking 30 mg. of methoxsalen (8-MOP) per day.

We have also administered methoxsalen (without ultraviolet irradiation) to one normal subject continuously for 13 months. This subject, a 50-year-old male, received a daily dose of 40 mg. for 2½ months and 60 mg. daily for 10½ months. The following tests were done before the start of the therapy and repeated at three-month intervals: cephalin-cholesterol flocculation, sulfobromophthalein, thymol turbidity, indirect, direct, and total bilirubin, and urine urobilinogen. All findings were normal before administration of the drug and remained within normal limits during the trial periods.

Side-effects.—In the placebo group of medical students, one subject reported epigastric distress during the first three days of the experiment, another developed vertigo during the first part of the experiment, and a third experienced a serous nasal discharge immediately after taking the placebo capsules. In the group receiving methoxsalen, two subjects noted a slight increase in beard hair growth, and one reported "peptic ulcer" symptoms, which disappeared as the therapy was continued.

One of the subjects, who had received methoxsalen for three months, later consulted an ophthalmologist for a routine eye examination and was *found to have an elevated ocular tension. This* subject was found to have a rare, nonfamilial type of glaucoma, known as pigmentary glaucoma. Each *of the remaining* 12 subjects was given a complete ocular examination, and none was found to have elevated ocular tension or any other abnormal ocular finding. It was the opinion of the department of ophthalmology that the occurrence of glaucoma in this subject was a coincidental finding unrelated to the drug therapy. However, the possible role of orally ingested methoxsalen in the production of pigment changes in the eye has been apprehended, and eye examinations are being made in patients receiving the drug. In addition, we are attempting to produce pigment changes in brown eyes of guinea pigs with orally given methoxsalen and exposure to long-wave ultraviolet irradiation. We have not been able to detect methoxsalen in aqueous humor from the anterior chamber, and guinea-pig eyes exposed daily for nine months under the above conditions have not shown any changes.

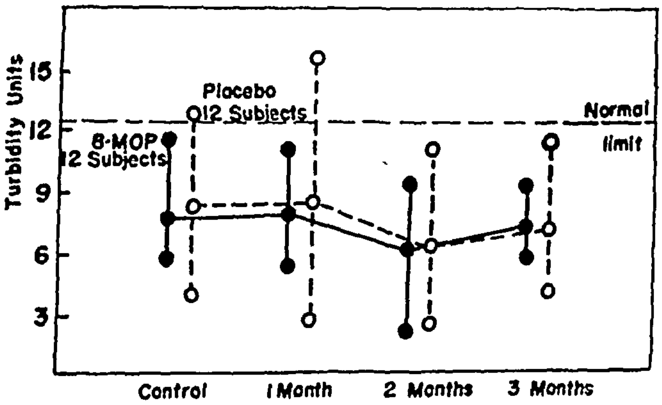


Fig. 4.—Means and extremes of zinc turbidity reactions determined at monthly intervals to compare 12 subjects taking placebo with 12 taking 30 mg. of methoxsalen (8-MOP) per day.

Comment

Except for Elliott's report in 1956,[1e] there has not been a study of liver function in patients or normal subjects receiving methoxsalen. As was mentioned above, the two abnormal results in sulfobromophthalein tests obtained in Elliott's series cannot be interpreted because there are no available data on the test findings prior to administration of the drug. Results from the cephalin-cholesterol flocculation tests reported by Lerner and associates in 1953 [1d] are all within normal limits.

It is recognized that the battery of liver function measurements could have been extended indefinitely, but it was felt that a selection of tests encompassing both excretory function (sulfobromophthalein) and protein function (cephalin, zinc, and thymol) would offer a fair measure of the state of liver cell function. Tests related more specifically to bile cell function were not performed, but abnormally colored urine and jaundice were never noted clinically. Jaundice, moreover, has never been reported in subjects receiving methoxsalen where other causes have been satisfactorily eliminated.

Although a selected profile of liver function tests and blood constituents relating to liver function were within normal limits throughout the course of administration of methoxsalen, we cannot yet conclude that the drug is safe for the general population. Since this study shows that none of the 12 subjects receiving methoxsalen developed a change in liver function, it is possible to state with 95% confidence only that no more than 27% of the population comparable to these subjects may develop a change in liver function. In other words, anywhere from 100% to 73% of persons receiving 30 mg. daily or orally given methoxsalen will not have a change in liver function as detected by the tests used in this study. The small sample size limits the sensitivity of the experiment and will not permit a more precise statement. To be at all certain of a negative effect of a drug for 99% of the general population would require an experimental group of at least 450 subjects.

Summary

Four liver function tests were performed serially in 24 normal human subjects before, during, and after daily administration of 30 mg. of methoxsalen (8-methoxypsoralen) for a period of three months along with casual exposure to ultraviolet irradiation to 12 of the subjects, the remaining 12 subjects receiving placebos. A double-blind experiment design was used. There was no significant difference in the liver function tests in the two groups. No subject had a change in liver function tests that would indicate liver damage.

Statistical analysis of the data indicates that, with the sample size used, it is possible to state with 95% confidence that 73% of young healthy males receiving a daily dose of 30 mg. of methoxsalen with casual ultraviolet irradiation for three months will not develop a change in liver function as detected by the tests used in this study (cephalin-cholesterol flocculation, sulfobromophthalein, and thymol and zinc turbidity). Nothing can be inferred about the probability of · change in liver function tests in occasional subjects up to 27% of the normal population or in subjects who have preexisting abnormal liver function. Six of seven subjects who received methoxsalen during the spring noted an augmentation of their response to sunlight, while none of the six subjects receiving the placebo noticed any difference in erythema or pigmentation.

3181 S. W. Sam Jackson Park Rd. (Dr. Fitzpatrick).

Drs. Carl E. Hopkins and Farrington Daniels Jr. aided in experimental design and statistical analyses in this study.

This study was supported by the Paul B. Elder Company, Bryan, Ohio.

The methoxsalen and placebo used in this study were supplied by the Paul B. Elder Company, Bryan, Ohio.

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J.A.M.A., July 26, 1958

TRIAMCINOLONE IN THE TREATMENT OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Twenty-nine patients with systemic lupus erythematosus were treated with a new synthetic, unsaturated prednisolone derivative, triamcinolone, for as long as 11 months. This hormone is 1.3 times as powerful as prednisone and 4.4 times as potent as hydrocortisone as an anti-inflammatory agent. The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids. There was a disappearance of all the clinical and laboratory abnormalities produced by the disease, with the exception of long-standing renal involvement. A major difference between triamcinolone and other steroids was a tendency, in 18 patients, toward progressive gradual weight loss, averaging 7.8% of initial body weight. The cutaneous side-effects, particularly Cushingoid appearance, hirsutism, and striae, were more marked than those with older steroids. The most serious side-effect was muscle weakness, which appeared in six patients from 4 to 32 weeks after start of triamcinolone therapy. Fourteen patients had received prior steroid therapy with all the older anti-inflammatory hormones and seven of them were better controlled and felt better with triamcinolone than with steroids used perviously.

During the past eight years, 275 patients with various forms of systemic lupus erythematosus have been treated under my supervision with salicylates, antimalarials, and steroids.[1] For the past 11 months, I have had the opportunity to study a group of 29 patients with systemic lupus erythematosus who required steroid therapy, using a new synthetic, fluorinated, unsaturated, anti-inflammatory hormone, triamcinolone (Aristocort). Chemically, this substance is 9α-fluoro-16α-hydroxyprednisolone.[2] The aim of this report is twofold. The first is to review experiences with this new agent and to compare the results with those produced by older steroids, and the second is to present the data obtained from performing routine gastrointestinal x-rays, gastric analyses, and 24-hour urinary uropepsin determinations before and during treatment with this new steroid in order to assay its ulcerogenic tendency and effects on gastric secretions.

Description of the Disease

Systemic lupus erythematosus is a chronic disease similar in clinical picture and course to rheumatic fever and rheumatoid arthritis. Eighty-eight per cent of the patients with this illness are females. The disease characteristically is subject to many remissions and exacerbations. In one detailed study of the occurrence of spontaneous remissions prior to steroid therapy, 38.7% of the 163 patients reported on had had at least one such illness-free episode before specific treatment.[1a]

The problem of diagnosis in this ailment is rendered difficult by its protean manifestations and by the fact that there is no classic pattern of the disease. Any system initially may be affected and heal, and months or years later the same or another area may be involved.

In one series of 62 patients, 34% developed arthritis, usually of the rheumatoid type initially; however, by the time the diagnosis was made, at least 90% had had similar symptoms.[3] The arthritis may vary from mere arthralgia to joint effusions and, in the later stages, classic rheumatoid deformities. Cutaneous eruptions of various types across the cheeks and bridge of the nose were presenting symptoms in 16.1%. These lesions may vary from the typical classic scaly erythematous eruptions of systemic lupus erythematosus to small, atypical, discoid lupus-like plaques. Cutaneous eruptions, as initial symptoms, appeared elsewhere on the body in 11.3% of the patients. These lesions varied in appearance from maculae to bullae. Other presenting manifestations included such diverse entities as Raynaud's phenomenon, hemolytic anemia, pleurisy with and without effusion, false-positive serologic tests for syphilis, pericarditis, fever, cachexia, renal disease, and epilepsy.

The key factor suggesting systemic lupus erythematosus as the cause of the above-described changes rather than a more common etiology is the occurrence of multisystem disease in these patients. A thorough history must be obtained, and when an individual, for example, has atypical rheumatoid arthritis with pleural effusion, unusual skin lesions, and renal involvement, systemic lupus erythematosus must be considered. The changes in these systems may not be concurrent but may occur years apart. For example, the illness may affect one system, such as the skin, with discoid-like lesions and

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fully heal; then, years later, it may produce pleuropericarditis without a cutaneous relapse. The occurrence of this type of multisystem disease should suggest systemic lupus erythematosus. In 80% of typical clinical cases, the diagnosis can be confirmed by finding L.E. cells, which, in my experience, are pathognomonic of the disease.[4] This concept of the specificity of this test is agreed on by some [5] and disagreed on by others.[6] If cutaneous lesions are present, skin biopsy is of value in confirming the diagnosis in another 10%. The diagnosis in the final 10% often rests only on clinical grounds. The proof that this type of multisystem disease is a distinct entity is that at autopsy almost all these patients show the classic features of systemic lupus erythematosus.

Steroid Therapy

Once the diagnosis of systemic lupus erythematosus is made, the type of treatment instituted depends entirely on the clinical severity of the illness. If the presenting problem is a false-positive serologic test for syphilis in an asymptomatic patient who has perhaps a few L.E. cells, then no therapy is necessary other than close observation of the patient. If the main complaint is mild rheumatoid arthritis or a rheumatic fever-like picture, this often can adequately be controlled by modified bed rest and salicylates, which should be increased in amount to the point of salicylism. The frequent use of these drugs should be encouraged, since they reduce the requirements for antimalarials and steroids. None of the patients in this study have been allergic to them. An increased amount of bed rest is usually helpful in controlling symptoms in the active stages of the disease, in addition to other treatment. If salicylates and rest fail or if cutaneous lesions are present, then antimalarial therapy should be instituted. When both these measures are inadequate or if the patient either is critically ill or has neurological or renal involvement, steroid treatment should be started.

Chemical Configuration of Triamcinolone.—Figure 1 illustrates the structure of triamcinolone alcohol compared to that of some of the older steroids. During the earlier part of the study, the diacetate ester was utilized (acetate radical on carbons 16 and 21). The structure of the alcoholic form is similar to that of prednisolone with the addition of a fluorine atom at the 9α position and a hydroxyl group at the 16α position. Fluorination greatly increases both the mineralcorticoid and glucocorticoid effects of all steroids; however, the salt-retaining effect is relatively much more increased. With the addition of a hydroxyl group at carbon 16 there is again elimination of the sodium-retaining effect of fluorination without much loss of the increased anti-inflammatory potency.[2]

Use of Triamcinolone.—The principles involved in using triamcinolone are identical with those in therapy with older agents.[1] If there is no clinical improvement (which is best judged by the temperature response in patients with acute cases in 24 to 48 hours), then the dose of steroids should be increased by amounts of 25 to 100%, depending on the urgency of the situation, until a therapeutic response occurs. As much as 3,500 mg. per day of cortisone has been used in treating an acute exacerbation of lupus erythematosus, with a successful outcome. There are no fixed limits of the dosage required to produce remissions; however, in several cases where there was no clinical response after several days' treatment with 3,500 mg. per day of cortisone or its equivalent in other steroids, increasing the dose beyond this point did not change the fatal outcome.

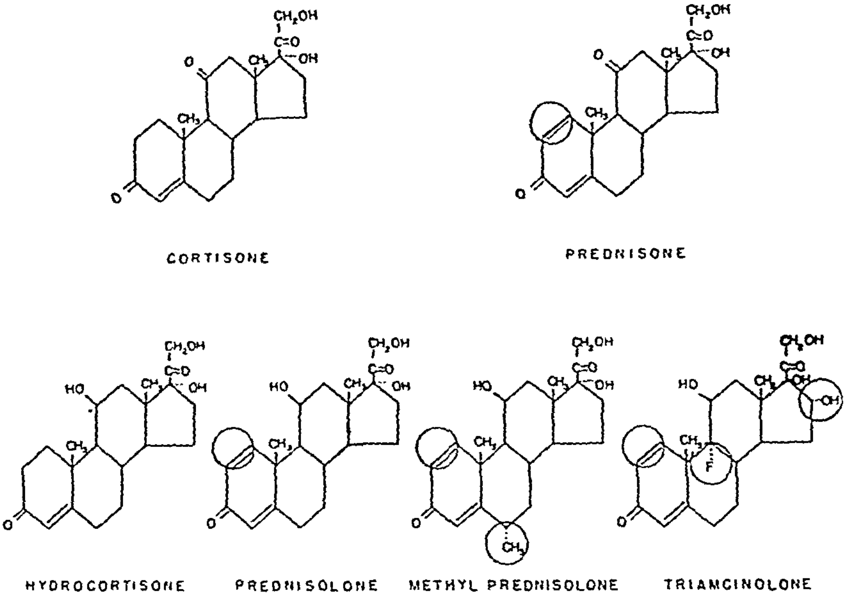

Fig. 1.—Structural formulas of commonly used anti-inflammatory hormones. Encircled areas denote significant differences between hormones. In triamcinolone, note 9α-fluoro and 16α-hydroxy groups which make this substance quite different from other steroids.

It is no longer necessary with the newer unsaturated steroids to routinely induce overt Cushingoid changes in the first 14 days of treatment.[1c] If neurological disease due to vascular systemic lupus erythematosus is present, much larger doses should be used and a Cushingoid appearance should be induced as quickly as possible in order to block progression of this change and initiate healing, which usually occurs.

Once the patient is afebrile and the symptoms controlled, the amount of medication must not be reduced until there is general improvement in the laboratory changes, as well as in the clinical picture of the patient. It is advisable to continue high dosages of steroids until all the abnormal physical findings, such as pleural effusion, pericarditis with effusion, and other active evidences of inflammation, subside. Advanced renal disease is the one exception that will not be benefited by continued treatment with large amounts of these hormones. The acute toxic nephropathy, with elevation of the nonprotein nitrogen level to approximately 100 mg. per 100 cc., will usually benefit from steroids, particularly if hypertension is absent. The nephrotic syndrome due to systemic lupus erythematosis will often improve. If there is no improvement in the renal lesions after two months of adequate steroid therapy with production of a Cushing state, then other modes of treatment, such as nitrogen mustard, must be considered.[1a]

TABLE 1.—*Clinical Data on Twenty-nine Patients with Systemic Lupus Erythematosus Treated with Triamcinolone*

	Range	Median	Mean
Age, yr.	11-57	32	33.7
Duration of disease, mo.	6-240	78	92
Duration of all steroid treatment including triamcinolone, mo.	1-80	27	28.2
Duration of triamcinolone therapy, mo.*	0.2-10.5	4	4.3
Dosage, mg. per day			
Initial (11 cases)	4-40	18	20.6
Maintenance (26 cases)†	8-96	18	26.0
Triamcinolone therapeutic ratio‡			
with hydrocortisone (9 cases)	1.0-7.5	4.5	4.4
with prednisone (5 cases)	0.75-3.3	1.2	1.3
with prednisolone (1 case)	1.0		
with cortisone (1 case)	3.1		

* Total patient-months, 125.2.

† Majority of these patients had active disease not well controlled by other steroids at time of transfer to triamcinolone.

‡ Therapeutic ratio = amount of drug required to produce equal anti-inflammatory effects on milligram for milligram basis, determined by dividing amount of triamcinolone required for maintenance into amount of older steroids. To ascertain dosage of triamcinolone to use in transfer, divide therapeutic ratio into one; for example, with hydrocortisone the therapeutic ratio is 4.4, and the factor is 1 ÷ 4.4 = 0.23 (23%) of dose of hydrocortisone.

When the hemoglobin level has become almost normal and the abnormal physical findings have disappeared, the steroid dose is reduced by decrements of about 10%. There should be a waiting period of four to seven days or longer to observe signs of relapse. Mild exacerbations with slight return of symptoms often appear within 24 hours—the so-called rebound phenomenon. This subsides spontaneously in a few days without dosage elevation if the amount of medication has not been reduced below the critical maintenance level so that a true relapse occurs.

The clinical picture and hemoglobin level are used as the major guides to steroid therapy. If significant renal involvement is present, this is closely followed in order to determine when to reduce the dose. The sedimentation rate is never used as the main index to dosage, since it can remain indefinitely elevated in some patients despite complete clinical remissions requiring no steroids. The L.E. cell test is helpful in following the over-all picture of the disease but should not be used as a basis to determine therapy, since it requires several weeks for changes to occur and since many patients have persistently positive L.E. cell tests despite remissions requiring no medication.

Clinical Material.—Twenty-nine patients with active systemic lupus erythematosus were treated. The diagnoses were proved by finding L.E. cells in 25 cases (86%), by clinical picture and positive skin biopsy in 3 cases (11%), and by clinical picture alone in 1 case (3%). There were 22 females (76%) and 7 males (29%). The average total duration of their individual illnesses from the time of onset of disease to the time of writing this paper was 92 months; the median duration was 78 months. The disease in 4 patients was stabilized with steroid therapy at the time of transfer to triamcinolone, and 14 had exacerbations due to the disease in varying severity. Eleven patients had active disease and had not recently received other steroid therapy. The average age of these patients at the time of treatment was 33.7 years, with a median of 32 years. The average age of onset of illness was 26 years. The mean duration of total hormone therapy, including triamcinolone, was 28.2 months, and the median was identical. The duration of treatment with triamcinolone averaged 4.3 months, with a median of 4 months and a range of 4 days to a maximum of 10.5 months in two patients. The total experience was 125.2 patient-months of therapy (See table 1).

Methods of Therapy

Dosage.—The amount of steroid required varied entirely with the severity of the disease and the sensitivity of the patient to that agent.[1] In the 11 patients who received no previous therapy, attempts were made to judge the initial dosages on past experience, with the assumption, based on animal and prior human studies, that the potency of triamcinolone was a little greater than that of prednisolone or prednisone.[7] The starting doses in these patients varied from the addition of 4 mg. per day to the therapeutic regimen of a 19-year-old boy with mild arthritis, poorly controlled on salicylates and antimalarials, to a maximum of 40 mg. per day in three patients whose disease was active, with multisystem involvement. The estimation of the dosages in 9 of the 11 cases, on the basis of clinical experience and severity of the illness, was correct and required little modification for control of the exacerbations.

Five patients who had been on prednisone therapy were transferred to triamcinolone therapy. The dosage required for the same clinical effect was 0.8 times the amount of prednisone, or, in other words, the new steroid had a therapeutic ratio or potency

1.3 times as great as prednisone on a milligram basis. The range varied from 0.75 to 3.3 times as potent as prednisone (See table 1).

Nine patients whose disease was controlled by hydrocortisone with varying degrees of success were changed to triamcinolone therapy. The amount of the new steroid for equivalent maintenance was 0.23 times the dosage of hydrocortisone, or the potency of triamcinolone was 4.4 times as great as hydrocortisone on a milligram basis. The range in individual cases varied from 1.0 to 7.5 times as potent.

One patient was changed from therapy with 20 mg. per day of prednisolone to therapy with 20 mg. per day of triamcinolone with equally good control. In another case, due to a severe exacerbation of the disease, equivalent dosage could not be determined. An additional patient was transferred from therapy with 50 mg. of cortisone to therapy with 16 mg. of triamcinolone per day with good control.

Ten patients, during their course of treatment, were transferred from therapy with triamcinolone acetate to that with the alcohol without any difference being noted in the clinical effects. Theoretically, the alcohol is a 17% smaller molecule and should have been slightly more potent on a milligram basis.

Adjuvant Therapy.—All patients were on a diet with normal salt intake except four who had a problem with excessive edema due to renal involvement. They were placed on a 200-mg. sodium diet. There was no evidence of sodium retention in any patient, except in one who developed a trace of ankle edema with triamcinolone therapy. Supplementary potassium was not given. Low serum potassium levels were not detected even on a maximum dosage of 96 mg. per day.

A routine prophylactic ulcer regimen, as usually recommended for patients taking over 50 mg. per day of cortisone or its equivalent, was not used except when indicated.[8] An ulcer diet with anticholinergic drugs was continued in two patients who had a recent history of a duodenal ulcer. Two others who had epigastric distress from other steroids were also on a similar diet. Gastrointestinal series, uropepsin findings, and gastric analyses in these patients remained normal. Three additional patients received anticholinergic medicaments without an ulcer diet because of epigastric distress after medication. The same gastrointestinal studies in these patients were normal and remained so.

Gastrointestinal Studies.—Sixteen patients had upper gastrointestinal x-rays before and every one or two months during treatment. The dosage of triamcinolone in these cases varied from 4 mg. per day to as much as 96 mg. per day. One patient had a known active duodenal ulcer proved by x-ray prior to institution of triamcinolone therapy. This healed with an ulcer regimen and the new steroid. One patient who had not been on a prophylactic ulcer regimen developed an acute superficial duodenal ulcer with gross bright red blood in the stool while taking 96 mg. per day of triamcinolone for three weeks. This was during the sixth month of high-dosage steroid therapy. The ulcer healed with a vigorous ulcer regimen and continuation of the same dose of triamcinolone. Findings from x-ray studies in the other patients were all normal. No changes were noted during the course of treatment with the new steroid. Bollet and co-workers found an incidence of 22% of new peptic ulcers with x-rays in patients similarly treated with prednisteroids, without a prophylactic ulcer regimen.[9]

Gastric analyses were performed in nine patients before and every two months during treatment with triamcinolone. Free and total acidity values were determined before and after subcutaneous injection of 0.1 mg. per 10 kg. of body weight of histamine phosphate. Specimens were drawn every 10 minutes after the injection for a total of 40 minutes. No significant changes were noted in any of the patients, including the patient who had proved duodenal ulcer which was healing under therapy and the one who developed an acute ulcer.

Twenty-four hour uropepsin determinations were performed by the method of West, in which the normal range is 15 to 40 units per hour.[10] Gray and associates [11] and Spiro and co-workers [12] have shown that excretion of uropepsin is increased with steroid or ACTH therapy, but others have not confirmed their findings.[13] Thirteen patients receiving triamcinolone were studied prior to and every few months during therapy. No significant changes were noted. Results were all within the normal range throughout the study in seven patients, including the one who developed an acute ulcer. Findings in three patients remained below normal initially and during steroid therapy, including those in one patient who received 32 mg. per day for five months. Findings in another three patients rose from subnormal levels to normal levels, including those in the patient with healing peptic ulcer.

Results of Therapy

The pattern of clinical improvement closely paralleled that obtained in systemic lupus erythematosus by previous treatment with corticotropin and the other anti-inflammatory hormones. The fever abated in 24 hours, joint pains disappeared in several days, and pleural effusion and cutaneous lesions subsided in one to two weeks. Retinal changes, anemia, adenopathy, and cachexia gradually improved over a period of several weeks. Renal abnormalities, including proteinuria, sediment changes, and nitrogen retention of short duration, often returned to normal during steroid-induced remissions. The long-standing renal lesions, particularly those associated with hypertension, are unaffected by hormone therapy but seem to be helped by nitrogen mustard.[8] Two patients had a severe nephrotic syndrome of systemic lupus erythematosus with uremia and hypertension. Both were unaffected by doses of as high as 80 mg. per day of triamcinolone. One patient with a mild nephrotic syndrome showed no diuresis with the new steroid but had excellent diuresis with nitrogen mustard (see case 1 below). Another patient with a low-grade nephropathy showed no change.

There was a decrease in weight in 18 patients, averaging 10.7 lb. (4.8 kg.) with a median of 9 lb. (4.1 kg.) and a maximum of 18 lb. (8.2 kg.). The average loss in terms of percentage of initial body weight was 7.8% with a median of 8.2%. The change was usually gradual and progressive over months rather than acute during the first few days of transfer to the new steroid. If there was much edema of nonrenal origin, this disappeared within a week. There was no loss of Cushingoid appearance induced by other steroids. The decrease is apparently a combination of several factors: (1) a complete lack of sodium retention of this steroid, even less than that of prednisone; (2) a great deal less appetite stimulation, the least of any of the steroids currently available; and (3) the most distressing factor, muscle wasting due to probable negative nitrogen balance, which will be discussed below. In six patients there was definite overt atrophy of extremity muscles and marked weakness along with increased Cushingoid appearance. This change did not occur in any of the seven males in the series who were given equally large doses of triamcinolone.

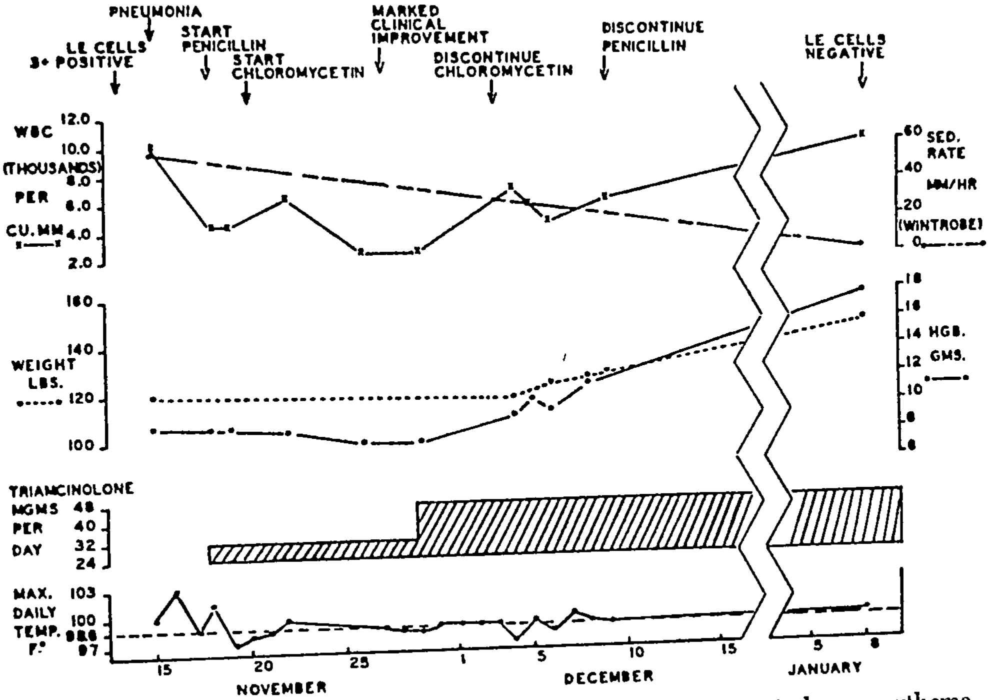

Fig. 2.–Clinical course of 44-year-old male patient with systemic lupus erythematosus treated with triamcinolone.

Weight increased in three patients, one male gaining 29 lb. (13.2 kg.) after six weeks of therapy (fig. 2). Weights were unchanged in eight patients.

Edema of 1+ degree in the presence of weight loss appeared in only one patient. There was no evidence of a low-sodium syndrome or potassium depletion clinically or by electrolyte determinations. Tests were performed whenever any symptoms appeared possibly related to these changes.

The mean blood pressure was unchanged in 20 patients. It decreased an average of 23 mm. Hg in 4 patients and increased an average of 29 mm. Hg in 5 patients. Two of these had uremia.

Changes in Laboratory Findings.–The hemoglobin level increased in 10 patients, averaging 2.7 Gm. per 100 cc. with a median of 2.2. Slight decreases occurred in three patients, averaging 1.1 Gm. per 100 cc.; in 16 instances the hemoglobin level was unchanged. In 14 of these patients the hemoglobin level had already been elevated to normal levels by prior steroid treatment.

White blood cell counts increased an average of 5,060 per cubic millimeter in 10 patients, with a median of 4,100. It was unchanged in 19 instances and decreased in none of the patients.

The sedimentation rate (Wintrobe) decreased in nine patients an average of 23.7 mm. per hour, with a median of 23. It increased in four patients an average of 28 mm. per hour. There was inadequate data in six cases.

L.E. cell tests, performed by the rotary technique, demonstrated a decrease in positivity in seven cases and an increase in two cases.[14] The cells fully disappeared in four patients within a minimum of four weeks. L.E. cells were unchanged in five patients and remained absent throughout therapy in seven patients, five of whom had had L.E. cells prior to previous therapy. Inadequate data were available for four patients.

Side effects.–The most serious side-effect of triamcinolone has been muscle weakness. This steroid also produces an increased severity of cutaneous changes, such as Cushingoid appearance, acne, hirsutism, and striae, than existed with older hormones of this type. There has been no problem with mineralcorticoid effects, such as salt retention or hypertension, except as noted above.

In table 2 is reviewed the side-effects, with a comparison of triamcinolone with prednisone and prednisolone. Only five patients in the trimacinolone group had the benefits of prednisteroid therapy prior to transfer to therapy with the newer hormone, so that the two groups are somewhat comparable, since they either were untreated prior to the steroids or were on cortisone or hydrocortisone therapy for the most part. The incidence of Cushingoid appearance with moon face is quite similar in both groups, whether therapy is initiated with ether agent. Severe hirsutism was noted in 21% (6 cases) in the triamcinolone group as against 3% in the prednisteroid group. Hirsutism appeared within four weeks on doses as low as 16 mg. per day and was much more marked than I have seen with the older steroids. At times the entire forehead was covered with hair. No excessive hirsutism of this type was found in males. The medicament was withdrawn in one patient because of this (fig. 3).

Striae and ecchymoses were more severe and common with the newer steroid, being prominent in 14% as against 3% with prednisteroids. Edema accumulated in only one of the patients on triamcinolone therapy and in 6% of the prednisteroid group. Two patients in the triamcinolone group noted epigastric burning after taking the medicament. In one it cleared while taking the medicament with antacid for several weeks, and in the other it spontaneously disappeared. Neither patient showed significant changes in the gastrointestinal studies. One patient in the prednisteroid group developed similar epigastric symptoms despite a prophylactic ulcer regimen. Another patient on triamcinolone therapy developed an acute peptic ulcer. Routine prophylactic ulcer therapy was not employed in the triamcinolone group, whereas it was in the prednisteroid group.

TABLE 2.—*Side-effects of Triamcinolone Compared with Those of Prednisone and Prednisolone in Comparable Groups of Patients*

Cushingoid Appearance	Patients Receiving Triamcinolone No	Patients Receiving Triamcinolone %	Patients Receiving Prednisone or Prednisolone,[1b] %
After transfer from older steroids			
Increased	4	14	14
Decreased	0	0	5
Unchanged	4	14	17
Initial appearance after starting triamcinolone as first steroid	4	14	15
Initial appearance after transfer to triamcinolone from other steroids	1	3	0
None at any time with triamcinolone	16	55	51
Total who developed or maintained Cushingoid features	13	42	42
Marked hirsutism	6	21	3
Acne	5	17	16
Striae, marked	4	14	3
Ecchymoses, marked	4	14	3
Edema	0	0	6
Diabetes mellitus, severe	0	0	6
Epigastric distress	2	6	3
Muscle weakness	6	19	0
Peptic ulcer*	1	3	3

*Only patients receiving prednisone and prednisolone were treated with prophylactic ulcer regimen.

The most serious side-effect of triamcinolone therapy was the appearance of profound muscle weakness, particularly in the extensor muscles of the legs and occasionally in the deep muscles of the back. The patients were characteristically unable to rise from a chair without using their hands or to climb stairs without holding on to the banister. If asked to squat down, they could not rise to a standing position unaided. These symptoms appeared from 4 weeks to as long as 32 weeks after the start of therapy. The average time of appearance was 13 weeks, with a median of 5 weeks. They appeared on a minimum dose of 12 mg. per day. There did not appear to be a relationship between the largest doses and the development of this side-effect. The onset of this change was quite insidious, but, when fully developed, it was profound and necessitated cessation of the steroid therapy in all six cases. No males developed this syndrome. Prior to the appearance of weakness in all the patients, there seems to have been a severe Cushingoid appearance with definite atrophy of the extremity muscles. Weakness in the upper extremity was not as evident. Electrolyte studies in four cases showed the serum sodium and potassium levels to be normal. Two patients were transferred to prednisone and four to hydrocortisone therapy in equivalent dosages. About two weeks after transfer, their strength gradually began to return to normal. One of the patients had a transitory pares-

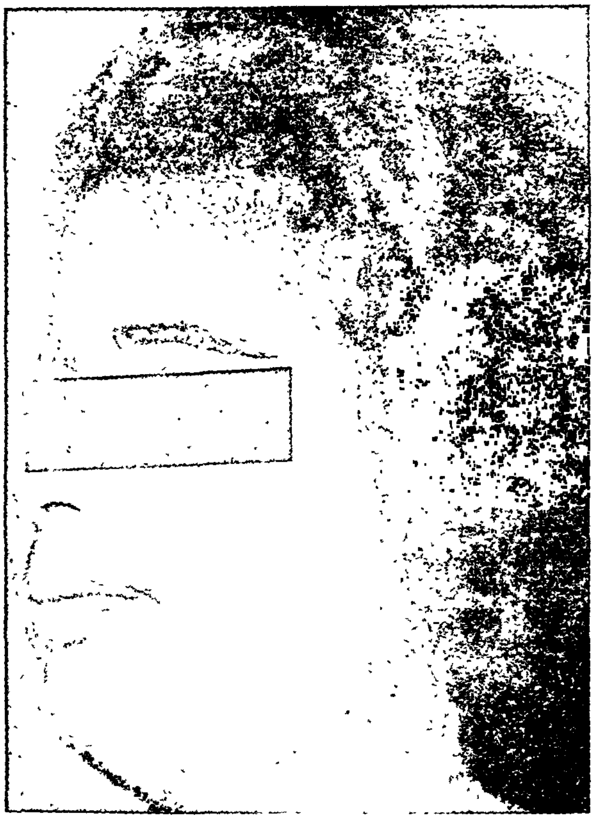

Fig. 3.—Excessive hirsutism produced by 16 mg. of triamcinolone per day within four weeks in a 16-year-old girl.

thesia for one day in her legs, and she could have had primary weakness due to vascular systemic lupus erythematasus. None of the other patients had any sensory changes. Reflexes were intact and active in the legs. These changes were similar to the quadriceps weakness seen in patients with hyperthyroidism and myasthenia gravis.

Case 1 illustrates the appearance of muscle weakness while the patient was receiving triamcinolone, as well as the refractoriness of the renal lesion to diuresis without the aid of nitrogen mustard.

Report of a Case

CASE 1 (fig. 4).—A 31-year-old woman became ill in March, 1954, with butterfly area rash, weight loss, arthralgia, and pleuritic pain. A skin biopsy was diagnostic of lupus erythematosus, and the patient was placed on therapy with 75 mg. per day of cortisone with only moderate relief of symptoms. When first examined in November, 1954, she showed a slightly Cushingoid appearance and had a blood pressure of 150/85 mm. Hg. Her weight was 112 lb. (50.8 kg.). A grade 2 blowing systolic murmur was present in the pulmonary area. The remainder of the physical examination showed normal findings. There was no edema. Laboratory studies at this time revealed a normocytic anemia, with a hemogloblin level of 11.2 Gm. per 100 cc. The sedimentation rate (Wintrobe) was 56 mm. per hour. The L.E. cell preparation was 4+. Urinalysis showed 4+ albuminuria and sediment containing many hyaline and granular casts and oval fat bodies. Urine protein level was 8.5 Gm. per 24 hours. The blood urea nitrogen level was 42 mg.%, and the cholesterol level was 280 mg.%. The phenolsulfonphthalein finding in 15 minutes was 26% and total in two hours was 77%. She was transferred from cortisone therapy to therapy with 20 mg. of hydrocortisone four times daily. The patient received 20 mg. of nitrogen mustard intravenously. By February, 1955, there had been no change in the urine, although the blood urea nitrogen level had decreased to 26 mg.%. She received another 20 mg. of nitrogen mustard. During the following two months, the albuminuria decreased to 2+, and the urinary sediment showed a marked decrease in abnormal elements. Because of her Cushingoid features, she was transferred to prednisone therapy, without a change in her appearance. By February, 1956, the urine showed 1 to 2+ albumin and about 30 red blood cells per high power field without casts. The blood urea nitrogen level had decreased to 14 mg.%.

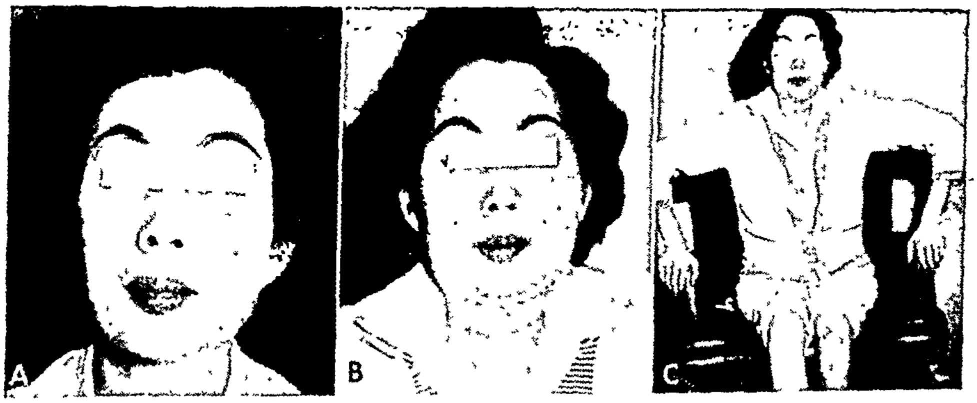

Fig. 4 (Case 1).—Patient with systemic lupus erythematosus: *A*, prior to triamcinolone therapy, Oct. 29, 1957; *B*, after six weeks of triamcinolone therapy, 40 mg. per day (Dec. 10, 1957), note marked Cushingoid features; *C*, note characteristic position taken by patient, in order to lift herself from chair, and large ecchymotic lesion on left knee.

By May, 1956, the patient was asymtomatic and urinalysis was unchanged. Therapy with all steroids was stopped. In November, 1956, gross hematuria suddenly appeared, with morning periorbital edema and low-grade fever. Microscopic examination of urine revealed red blood cells and granular casts. The blood urea nitrogen level was 45 mg.%; the cholesterol level was 160 mg.%. Therapy with 80 mg. per day of prednisone was begun, and the patient had a diuresis resulting in a loss of 6 lb. (2.7 kg.). After four days, the urine returned to normal in color and the red blood cells were reduced to their previous level of 40 per high power field. In May, 1957, the patient felt well and again all steroids were withdrawn. Her urine showed 1 to 2+ albumin and a moderate number of red cells and casts of various types.

On Oct. 29, 1957 (fig. 4*A*), the patient noted increasing periorbital edema in the morning and definite ankle edema. Her blood urea nitrogen level was 26 mg.%, and her urine protein level was again 4+. Therapy with triamcinolone was begun at 10 mg. four times daily. By Nov. 9, 1957, the ankle edema had increased to 2+, and a dry cough had appeared. Striae were noted on the feet from the edema and steroids. The urine protein level decreased to 1+. Because of a progressive weight gain of 3 lb. (1.3 kg.) and edema, 1 Gm. of chlorothiazide (Diuril) given twice daily was added to the therapy without any marked response. Three days later the dose of the diuretic was increased to 1 Gm. four times daily without any change in weight. At this time, the blood urea nitrogen level was 46 mg.%, and the cholesterol level was 617 mg.%. On Nov. 14, 1957, 20 mg. of nitrogen mustard was given intravenously, and within two days the patient lost 4 lb. (1.8 kg.) of edema fluid. During the next 12 days a total of 15 lb. (6.8 kg.) of edema fluid was lost. On Nov. 19, 1957, the dose of chlorothiazide was reduced to 0.5 Gm. four times daily and omitted completely the following week. There was no apparent affect of this diuretic on the edema. On Nov. 29, 1957, the blood urea nitrogen level was 29 mg.% and only a trace of edema was left. About this time the patient noted the insidious onset of muscle weakness with inability to rise from a chair without using her hands to lift herself up. During the next few weeks this progressed to the point that the patient could not climb stairs without pulling herself up on the banister. When examined again on Dec. 10, 1957 (fig. 4*B* and *C*) she showed markedly Cushingoid features, with apparent atrophy of arm and thigh muscles, and she was completely unable to rise from a chair without using her arms. When she was asked to raise herself from a squatting position, she collapsed to the floor and was unable to lift herself without help. Triamcinolone (32 mg. per day) was withdrawn and predisone given in a dose of 20 mg. per day. (Although serum electrolyte levels were not determined in this patient, studies of serum electrolytes, including potassium, showed normal findings in four of the six patients in whom these tests could be done.) Within three weeks her strength had gradually improved so that she could rise from a chair unaided. Because of persistence of her urinary abnormalities, with rise in albuminuria to 4+, the predisone dosage was increased to 40 mg. per day. During the following week her ankle edema increased to 2+. The weakness did not return, although the patient took this larger dose for an additional three weeks.

Profound muscle weakness appeared six weeks after the start of triamcinolone therapy and disappeared gradually three weeks after the change to prednisone in equivalent doses. This patient had received cortisone, hydrocortisone, and prednisone in equally high doses previously without a similar event occurring. The case also demonstrates the effectiveness of nitrogen mustard as a diuretic agent with amelioration of the renal lesion of lupus erythematosus after steroids and chlorothiazide failed. In addition, this patient shows the benefit of steroids for acute glomerulonephritis due to systemic lupus erythematosus.

Comment

Triamcinolone seems to have a definite place among the anti-inflammatory agents. It has less sodium-retaining ability than other steroids currently available. It has no significant gastrointestinal stimulating activity, which should make it useful in patients who have had problems with peptic ulceration on therapy with older steroids. The development of an acute duodenal ulcer in one patient without changes in the gastric analysis and uropepsin excretion suggests that the mechanism of ulceration of the stomach and duodenum may not be related to acid or pepsin secretion but may be caused by other factors, such as decrease in viscosity of gastric mucous or perhaps retardation of normal healing by the steroids.[15]

Many patients are helped more by this steroid than by the older ones. Fourteen patients had received prior therapy with all the older anti-inflammatory hormones, and 7 of these were better controlled and felt better with triamcinolone than with previously given steroids. Male patients show no Cushingoid features with this steroid, even in doses as high as 48 mg. per day for six weeks. In men this may be the agent of choice.

The most serious side-effect of triamcinolone in patients with systemic lupus erythematosus has been muscle weakness. This has been found in about 10% of patients with rheumatoid arthritis treated with it.[7] In these patients it was only of minor degree. However, the dosages used were smaller than those used in this study. It is noteworthy that no cases have been found in males in this series, possibly due to the protective action of testosterone against the protein catabolic action of triamcinolone.

Unfortunately, this newer steroid has more cutaneous side-effects than the older hormones, so that it would not be the one of choice with which to initiate therapy in the average patient. Another disadvantage of this agent is that it, like the rest of the unsaturated steroids, varies greatly in potency from patient to patient. In some cases these hormones are equally potent with hydrocortisone on a milligram basis, and in others they are 10 times as powerful. Because of this great variability in dosage and individual unpredictability of action, I prefer to initiate treatment in the average case of systemic lupus erythematosus with hydrocortisone unless there is a problem of cardiorenal disease.

Summary

Twenty-nine patients with systemic lupus erythematosus were treated with a new synthetic, unsaturated prednisolone derivative, triamcinolone, for as long as 11 months. This hormone is 1.3 times as powerful as prednisone and 4.4 times as potent as hydrocortisone as an anti-inflammatory agent. The average dose for initiating therapy in a patient with a mild case of systemic lupus erythematosus was 20.6 mg. per day. The average maintenance dose used to control mild exacerbations of this disease was 26 mg. per day. There was no evidence of sodium retention or potassium loss. Routine sodium restriction, potassium supplementation, and prophylactic ulcer diet were not used.

Sixteen patients had upper gastrointestinal series done prior to and every one to two months during therapy with triamcinolone. There was evidence of peptic ulceration in only one patient, who received 96 mg. per day. Nine patients had gastric analyses with histamine performed before and about every two months during therapy with the new steroid. No significant changes were noted in these tests, even in a patient who developed an ulcer. Twenty-four hour uropepsin determinations were also done in thirteen patients prior to therapy and at similar intervals with the other tests. No abnormal increases were found, even in a patient with an acute ulcer.

The pattern of clinical improvement closely paralleled that obtained by previous treatment with older steroids. There was a disappearance of all the clinical and laboratory abnormalities produced by the disease, with the exception of long-standing renal involvement. A major difference between triamcinolone and other steroids was a tendency, in 18 patients, toward progressive gradual weight loss, averaging 7.8% of initial body weight. Some of this was fluid loss. There was no disappearance of a prior Cushingoid appearance produced by other steroid therapy.

The cutaneous side-effects, particularly Cushingoid appearance, hirsutism, and striae, were more marked than those with older steroids. The most serious side-effect was muscle weakness, which appeared in six patients from 4 to 32 weeks after starting triamcinolone therapy. There did not seem to be a relationship between dosage and this symptom. The profound muscle weakness, most marked

in the quadriceps groups, gradually cleared after several weeks of therapy with another steroid. No cases occurred among seven males in this series.

Fourteen patients had received prior steroid therapy with all the older anti-inflammatory hormones, and 7 of them were better controlled and felt better with triamcinolone than with previous steroids. Male patients show no Cushingoid features with this steroid, and for them this may be the steroid of choice.

Addendum

A total of 31 patients with systemic lupus erythematosus have been treated to date. The maximum duration of therapy is 14.5 months, in two cases. The patient-months of observation now total 166, with a mean duration of 5.4 and a median of 4.0 months. The clinical observations for the additional period show no changes from those described in the text above.

Only one patient in this series has developed any evidence of new peptic ulceration while taking triamcinolone as noted. This 11-year-old girl, who had not been on a prophylactic ulcer regimen, had the sudden appearance of bright red blood in the stool while taking 96 mg. of triamcinolone daily for three weeks. This was during the sixth month of high-dosage steroid therapy. A superficial duodenal ulcer, found by x-ray, healed with a vigorous ulcer regimen and continuation of the same dosage of triamincinolone. Because of a lack of general improvement despite a Cushingoid appearance, one month after the bleeding episode the patient was transferred to therapy with methylprednisolone (Medrol), 96 mg. per day, and anticholinergic drugs were withdrawn because of obstipation. Ten days later a similar bleeding episode occurred. Repeat gastrointestinal x-rays at this time were equivocal. The bleeding disappeared with reinstitution of anticholinergic medication and reduction of the dosage of methylprednisolone. Two weeks later the patient died, and at autopsy evidence of disseminated cryptococcosis was found, as well as the changes due to systemic lupus erythematosus. No evidence of gastrointestinal ulceration was noted at postmortem examination, nor could any other bleeding point be found.

Sixteen patients with systemic lupus erythematosus have been treated with methylprednisolone (Medrol). The average duration of therapy has been 2.9 months, with a median of 2.8 months and a maximum period of observation of 7 months in two cases. The total patient-months experience is only 47.3. The potency of this hormone is equal to that of prednisone on a milligram per milligram basis. The clinical results closely parallel those obtained from prednisone in the treatment of this disease.[1b] No distinct advantages of this steroid over the older ones have been noted. One patient, who had developed muscular weakness on therapy with triamcinolone which disappeared after transfer from this to therapy with hydrocortisone, was given methylprednisolone, 32 mg. per day. Within two months she had the identical recurrence of muscle weakness. Two weeks after retransfer to hydrocortisone therapy, her strength began to improve.

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This study was supported by grants from the Lederle Laboratories Division, American Cyanamid Co., the Attending Staff Association of the Los Angeles County General Hospital, and the National Lupus Erythematosus Foundation, Inc.

The triamcinolone used in this study was supplied as Aristocort through Dr. Christopher H. Demos of Lederle Laboratories Division, American Cyanamid Co., Pearl River, N. Y.

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CEREBRAL VASOSPASM—CLINICAL AND EXPERIMENTAL EVIDENCE

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Clinical and experimental observations indicate that the larger cerebral arteries in man are capable of vasoconstriction when subjected to certain types of artificially imposed mechanical stimuli. Vasodilatation can be induced by topical application of 2% procaine or 3% papaverine after dissection or test stimuli have caused vasospasm. Observations indicate that the basal cerebral arteries react to trauma as do other arteries of the body. This response to trauma appears to be the same whether the stimulus is mechanical during an experiment or is the result of a disease process, such as rupture of an aneurysm, perivascular hemorrhage, or, perhaps, other pathological conditions.

Cerebral arteries, such as those of the circle of Willis, unlike the smaller pial vessels,[1] are clearly subject to vasospasm, as demonstrated by angiography [2] and visualization during intracranial surgery.[3] Recognition of this sort of cerebral vasospasm, moreover, is often significant as to diagnosis and prognosis after hemorrhage from an intracranial aneurysm. Localized spasm, for example, may be the only angiographic clue to the location of a recently ruptured aneurysm when multiple aneurysms are present,[2c] while more extensive spasm is frequently a grave prognostic sign indicating the risk of permanent brain damage and, hence, the need for prompt intracranial surgery.[4] For these reasons and also because cerebral angiospasm may at times play a role in certain other circulatory disorders, such as migraine, vascular hypertension, and perhaps Bell's palsy,[5] the following studies were made dealing principally with the photographic demonstration and relief of vasospasm induced by dissecting or stroking branches of the circle of Willis in cat, dog, monkey, and man.

Clinical Data

Angiography frequently reveals vasoconstriction adjacent to an intracranial aneurysm that has recently bled.[2] Such vasoconstriction may occasionally be so severe and extensive as to cause hemiplegia or lead to serious cerebral edema that may prove fatal. The reversible character of this type of angiospasm has been demonstrated both by its disappearance on subsequent angiographic studies, including those made after surgical occlusion of an aneurysm (fig. 1), and by postoperative improvement in neurological signs.

We have found, as other neurosurgeons have also observed, that dissection of arteries of the circle of Willis during their exposure may result in local vasoconstriction,[3a] regardless of whether the operation is carried out under local or general anesthesia at normal body temperature or under hypothermia.[6] We have noted, in addition, that local application of 2% procaine or 3% papaverine to the constricted portion of the artery with a small cotton pledget may then result in vasodilatation. However, vasospasm already present as a result of hemorrhage from an aneurysm [3] may not always be relieved by topical applications of these drugs at operation.

From the Service of Neurological Surgery, the Neurological Institute, Presbyterian Hospital.

Experimental Data

Gentle trauma applied to branches of the exposed circle of Willis in the anesthetized cat, dog, or monkey by dissection of enveloping arachnoid membrane or by deliberate light stroking 5 to 15 times with an applicator or probe invariably results in promptly visible local vasoconstriction which lasts up to eight minutes and much longer after repetitive tests. Local application of either 2% procaine or 3% papaverine to the constricted artery results in prompt vasodilatation of these cerebral vessels (fig. 2). Of these two drugs, papaverine has the more effective vasodilator action. We, as well as others,[7] have also observed this effect on arteries of equivalent size elsewhere in the body. In addition, we have noted that papaverine generally results in greater enlargement of the arterial diameter than that of its resting state (fig. 2).

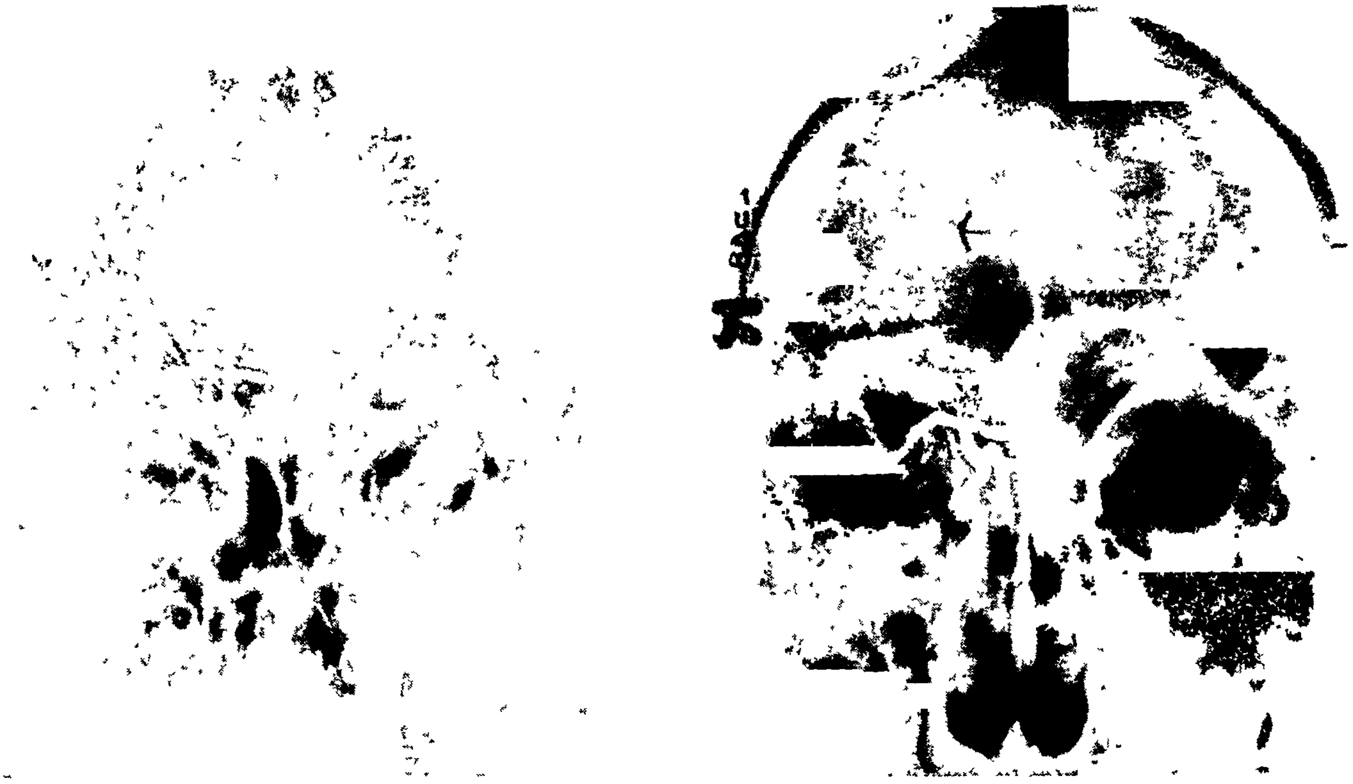

Fig. 1.—*Left*, vasospasm 12 days after hemorrhage from aneurysm of anterior communicating artery. Note diffuse spasm of intracranial portion of internal carotid and middle and anterior cerebral arteries, with marked constriction of anterior cerebral artery immediately proximal and distal to the aneurysm. (Angiogram photographs retouched for greater contrast.) *Right*, angiogram three and one-half weeks after intracranial clip occlusion of saccular aneurysm, showing enlargement of the previously constricted cerebral arteries to apparently normal caliber.

These effects have been demonstrated repeatedly in our experimental preparations (20 cats, 5 dogs, 1 monkey), regardless of body temperature, blood pressure, or the type of anesthesia, barbiturate anesthesia having been used in some experiments and intravenously administered succinylcholine (Anectine) with local 1% procaine infiltration for the craniectomy in others. Topical application of 2% procaine and, especially, 3% papaverine also serves to protect the tested artery from recurrent vasospasm on repeated stroking. Intracarotid injections of these drugs, however, was ineffective. The smaller arteries of the brain reacted with proportionately less vasoconstriction than the larger basal arteries when subjected to similar mechanical stimuli. This is in keeping with the report that still smaller vessels, such as the pial arteries, do not constrict after stimulation with an applicator,[1a] as we have also noted.

Comment

The clinical and experimental observations just described indicate that the larger cerebral arteries in man and three different species of animals are capable of vasoconstriction when subjected to similar types of artificially imposed mechanical stimuli. It was further evident that vasodilatation can be induced by topical application of 2% procaine or 3% papaverine after dissection or test stimuli have caused vasospasm. In the laboratory it was also found that, when these drugs were applied prior to test stimuli, the degree of vasoconstriction was less than that which could be induced in untreated vessels, suggesting a protective effect. Papaverine, regardless of whether or not procaine had already been applied, generally exerted more pronounced protective and vasodilator effects than procaine.

Since procaine acts primarily on nerves and nerve endings, and papaverine on smooth muscle, it is suggested that the observed changes in contractility of the larger cerebral arteries may be mediated both by their local intrinsic nerve supply[3a] and by their smooth muscle fibers, both in animals and in man.[8] Of these two factors, the smooth muscle response is evidently more powerful than neurogenic regulation of the caliber of cerebral arteries.

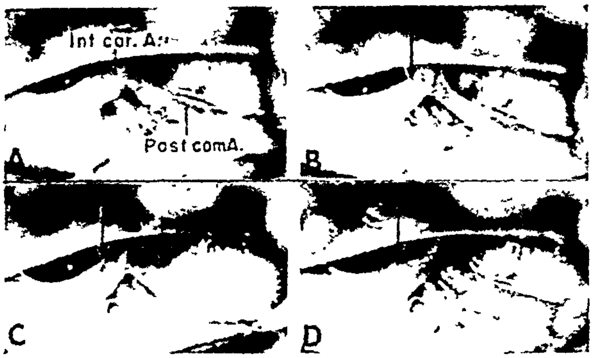

Fig. 2—Photographs of basal cerebral arteries of a dog exposed by brain retraction after craniectomy with use of local 1% procaine infiltration, intravenously administered succinylcholine (Anectine), and artificial respiration. Blood pressure remained constant. Similar vasospasm and vasodilatation have been demonstrated in cat, monkey, and man. Arrows point to internal carotid artery at site of stroking close to tentorial margin and posterior communicating artery. *A*, resting state of arteries after their exposure. *B*, vasospasm of internal carotid artery after stroking. *C*, vasodilatation after topical application of 2% procaine. *D*, further vasodilatation, now larger than resting size, after application of 3% papaverine.

These observations indicate that the basal cerebral arteries react to trauma as do other arteries of the body. This response to trauma appears to be the same whether the stimulus is mechanical during an experiment or is a result of a disease process, such as rupture of an aneurysm, perivascular hemorrhage, or, perhaps, other pathological conditions. In other words, vasospasm in the basal cerebral vessels can be an active process as a result of specific local stimuli.

Summary

Clinical and laboratory observations indicate that in animals and in man the larger arteries of the brain, such as those of the circle of Willis, are capable of vasospasm.

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ADENOIDS AND HEARING LOSS.—Adenoidectomies were performed on 100 children suffering from various degrees of conductive deafness. In every case conservative therapy, including antibiotics, local treatments, and, in some instances, irradiation with radium and x-ray, had failed. After operation, of 78 children tested within two weeks, 40% were cured of their hearing loss and an additional 42% were improved. At the time of the last audiogram taken on all 100 patients, 63 were cured and 33 were improved; 3 showed no change, and only 1 could be considered worse. Despite the absence of a control group, the proportion of cures and improvements seems considerably higher than could be explained on the basis of spontaneous resolution. It is concluded, therefore, that when conductive deafness, in a child with adenoid tissue, does not respond properly to conservative therapy, an adenoidectomy can often lead either to cure or to substantial improvement.—Joseph Sataloff, M.D., and Hyman Menduke, Ph.D., Adenoids and Hearing Loss in Children, *A. M. A. Journal of Diseases of Children*, May, 1958.

SURGICAL DIATHERMY (ELECTROTHERMIA) OF CANCER OF THE RECTUM

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Shortly after the publication by Strauss and others [1] of their favorable results following electrothermal coagulation of rectal cancer, one of us (R. T.) began to investigate seriously the merits of this form of therapy. Electrothermia was limited to nonulcerating lesions that were regarded as unresectable either after exploratory celiotomy or on a clinical basis, such as fixation, and in patients who were regarded as extremely poor risks for an abdominoperineal resection of the rectum. In the first series of 15 patients, only one tumor disappeared completely following electrothermal coagulation. On purely clinical grounds we could not explain why this tumor should have responded well when similar tumors in the remaining patients were unaffected by this modality. Continued clinical investigation in more than two score of other patients yielded the same end-results, namely, an occasional unexplainable brilliant success in the midst of discouraging failures in the preponderance of other patients. In fact, some patients were even made clinically worse after electrocoagulation by virtue of the increase of tenesmus or bleeding or both. After treatment some patients could not tolerate instrumentation, even diagnostic endoscopy, without regional anesthesia.

Even today, we still have great misgivings about treating rectal cancer by electrocoagulation, be'ause in most cases we are unable to remove the tire lesion for microscopic study (total biopsy) determine the presence or absence of invasiveness. Because of the flatness of many lesions, we are usually forced to resort to multiple fractional biopsies, which hardly ever permit, with any degree of exactitude or certainty, the detection of the extent of invasion into or beyond the muscularis mucosae, which we consider the determining line of invasion (fig. 1). As in the case of malignant transformation in adenomas [2] (a lesion we decidedly excluded from consideration in this paper), involvement of the lamina propria without invasion of the muscularis mucosae for the purposes of this paper is not considered invasive cancer. We are, however, mindful of the possible embolic route of dissemination of malignancy. It is known that cancer cells may fortuitously enter the lymphatic or blood vessels and thus cause regional or distant metastases without direct invasion of the muscularis mucosae or the intestinal wall.

The application of surgical diathermy (electrocoagulation) is described in four cases of rectal neoplasm. Biopsy specimens from the first patient were reported as showing a noninfiltrating adenocarcinoma without adenomatous tissue; after treatment by electrocoagulation the lesion was replaced by a scar, and there was no evidence of recurrence nine months later. In the second patient, biopsy led to the diagnosis of infiltrating adenocarcinoma; electrocoagulation was used because the poor general condition of the patient contraindicated more extensive surgery. Examination 11 months later yielded no evidence of malignancy. In the third, a sessile lesion in the rectum was diagnosed as infiltrating adenocarcinoma at biopsy; 14 months after electrocoagulation of the lesion sigmoidoscopy revealed normal mucosa at the site of the lesion. In the fourth patient, rectal pain of four or five years' duration led to sigmoidoscopy and the finding of an infiltrating carcinoma. This lesion was removed with a cold biopsy forceps, and the base was electrocoagulated; when last seen, the patient was free from gross evidence of rectal malignancy. The authors present evidence, however, that such favorable results from electrocoagulation in rectal cancer are exceptional. For the invasive type of lesion the authors continue to recommend the currently accepted surgical procedures, and they reserve electrocoagulation for those patients who are considered extremely poor surgical risks.

During the past decade, in private and in clinical practice, the value of electrothermal coagulation for the treatment of rectal cancer by a technique similar to the one described by Strauss and others [1] or Turnbull [3] has been reinvestigated. This form of therapy has been limited to (1) adenocarcinoma that is confined to the mucosa (superficial) (fig. 1*A*, 2*A*, 2*B*) in a patient who is either a poor risk for a serious operation or in one who refuses surgical intervention, usually colostomy, which is a

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rather uncommon occurrence nowadays, and (2) carcinoma which extends into the muscularis mucosae (fig. 1*B*) in patients who are regarded as poor risks for radical surgical intervention. Patients with ulcerating lesions who refuse operation or even those who are considered poor risks have, as a rule, *not* been treated by electrocoagulation.

Report of Cases

For illustrative purposes, the following description of several recent selected cases is presented:

Case 1.—A 62-year-old man had had multiple admissions to the Mount Sinai Hospital for a period of over 20 years. He had also been followed in the arthritis, diabetes, and peripheral vascular disease outpatient clinics over this period of time. In 1950, he had a cerebral vascular accident with resultant permanent paresis of his left arm and leg. In April, 1957, he reported intermittent bleeding per rectum of three to four months' duration as well as increasing constipation and tenesmus. Digital rectal examination and sigmoidoscopy revealed a flat but polypoid mass about 2 cm. in diameter that was located on the left posterolateral wall 9 cm. cephalad to the anal verge.

Several biopsy specimens (fig. 2*A* and 2*B*) of this lesion revealed noninfiltrating (superficial) adenocarcinoma (without adenomatous tissue). The patient was therefore admitted to the hospital on April 23, 1957, for definitive therapy. Because of his poor general physical condition and an unexpected finding of aleukemia, the rectal neoplasm was treated by electrothermia. On May 13, 1957, biopsy of the coagulated area revealed atypism of cells without evidence of malignancy. Repeated endoscopic examinations at two-month intervals showed a healed scar. The patient was last seen in January, 1958, at which time there was no gross or microscopic evidence of recurrence of the rectal lesion.

This is an instance of superficial cancer confined to the mucosa (fig. 1*A*). It is our present clinical feeling that this type of lesion, especially when located in the posterior and/or lateral walls of the rectum, may be treated conservatively. This is especially true in the presence of systemic contraindications to major surgery or when patients refuse surgical intervention.

Case 2.—A 64-year-old man first entered the Mount Sinai Hospital July 31, 1953, because of hemoptysis of seven months' duration. Bronchoscopy and roentgenography of the chest revealed a lesion in the lingular division of the left upper lobe, which, on biopsy, proved to be a squamous cell carcinoma and for which a left pneumonectomy was performed. Microscopy of the excised lung again revealed the presence of squamous cell carcinoma with early infiltration but without involvement of the lymph nodes.

The patient was readmitted to our hospital Nov. 23, 1956, because of the passage of black stools for one week and bilateral lower abdominal pain for one month; this pain radiated to the back but was relieved by defecation. He had been entirely free from pulmonary symptoms, but he developed increasing joint pain which was relieved by cortisone therapy. Roentgenography of the chest revealed a "coin lesion" in the right lower lobe. Double contrast barium enema showed a small, irregular, sessile defect, about 1 cm. in diameter, at the rectosigmoid. Sigmoidoscopy confirmed the presence of a rectosigmoidal sessile lesion. Microscopy of specimens removed by biopsy revealed infiltrating adenocarcinoma (fig. 2*C*). Laboratory studies revealed a hemoglobin value of 10.4 Gm. per 100 cc. of blood and a sedimentation rate of 107 mm. per hour. The latex fixation test for rheumatoid arthritis was strongly positive. The postoperative pulmonary lesion noted on roentgenography was presumed to be either a primary or metastatic neoplasm.

Because of this pulmonary finding and the patient's poor general physical condition, it was elected to treat the rectal malignancy by electrocoagulation. Endoscopic examination on Dec. 24, 1956, 10 days after electrocoagulation, revealed the usual superficial necrotic reaction. He was discharged Dec. 26, 1956. Sigmoidoscopy on Feb. 6, 1957, disclosed small heaped up nodules, 0.25 cm. in diameter, at the site of the previous coagulation; these, on biopsy, proved to be only fibrous tissue. The patient was last seen in November, 1957, at which time there was no gross evidence of rectal malignancy. The pulmonary lesion was, however, progressing in size, and there was gradual deterioration of the patient's general physical condition.

Case 3.—A 64-year-old man first entered the Mount Sinai Hospital on Oct. 28, 1953, because of hematuria and urinary frequency. Cystoscopy revealed a papillary carcinoma at the dome of the bladder. A partial cystectomy was performed, and pathological studies showed transitional cell carcinoma with early muscle infiltration. The patient was discharged Nov. 22, 1953, and subsequently received radiation therapy to the suprapubic area. On Feb. 12, 1955, recurrent carcinoma of the bladder was recoagulated. About this time the patient developed an acute coronary artery occlusion with infarction.

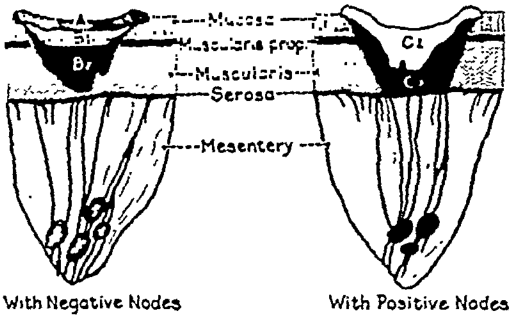

Fig. 1.—Modified Dukes classification: *A*, lesion is confined to mucosa; *B1*, lesion extends into muscularis mucosae, but not through it, with negative lymph nodes; *B2*, lesion extends through muscularis mucosae, without nodal involvement; *C1*, lesion of type *B1* or *B2* is limited to intestinal wall, with involved lymph nodes; *C2*, lesion extends through all layers of the intestinal wall, with postive lymph nodes. (Reproduced with permission from *The Surgical Clinics of North America* **35:**1295-1305 [Oct.] 1955).

On Jan. 11, 1956, he was readmitted to the hospital because of increasing dysuria. On rectal examination a mass was felt. Double contrast barium enema showed a possible polyp of the upper segment of the descending colon. Sigmoidoscopy disclosed a sessile lesion 2.5 cm. in diameter on the right posterolateral aspect of the rectum about 8 cm. cephalad to the anal verge. Biopsy of the rectal lesion revealed infiltrating adenocarcinoma. An electrocardiogram taken at this time still demonstrated myocardial disease associated with a bundle branch block. Cystoscopy revealed recurrent infiltrating cancer of the bladder. For these reasons, the rectal malignancy was treated by electrocoagulation. Ten weeks after coagulation of the rectal lesion, endoscopy revealed the rectum to be free from cancer.

On Jan. 11, 1957, the patient was readmitted because of another recurrence of the cancer of the bladder. At this time he began to complain of pain in the right shoulder. On March 12, 1957, on physical examination the liver border was felt two fingerbreadths below the right costal

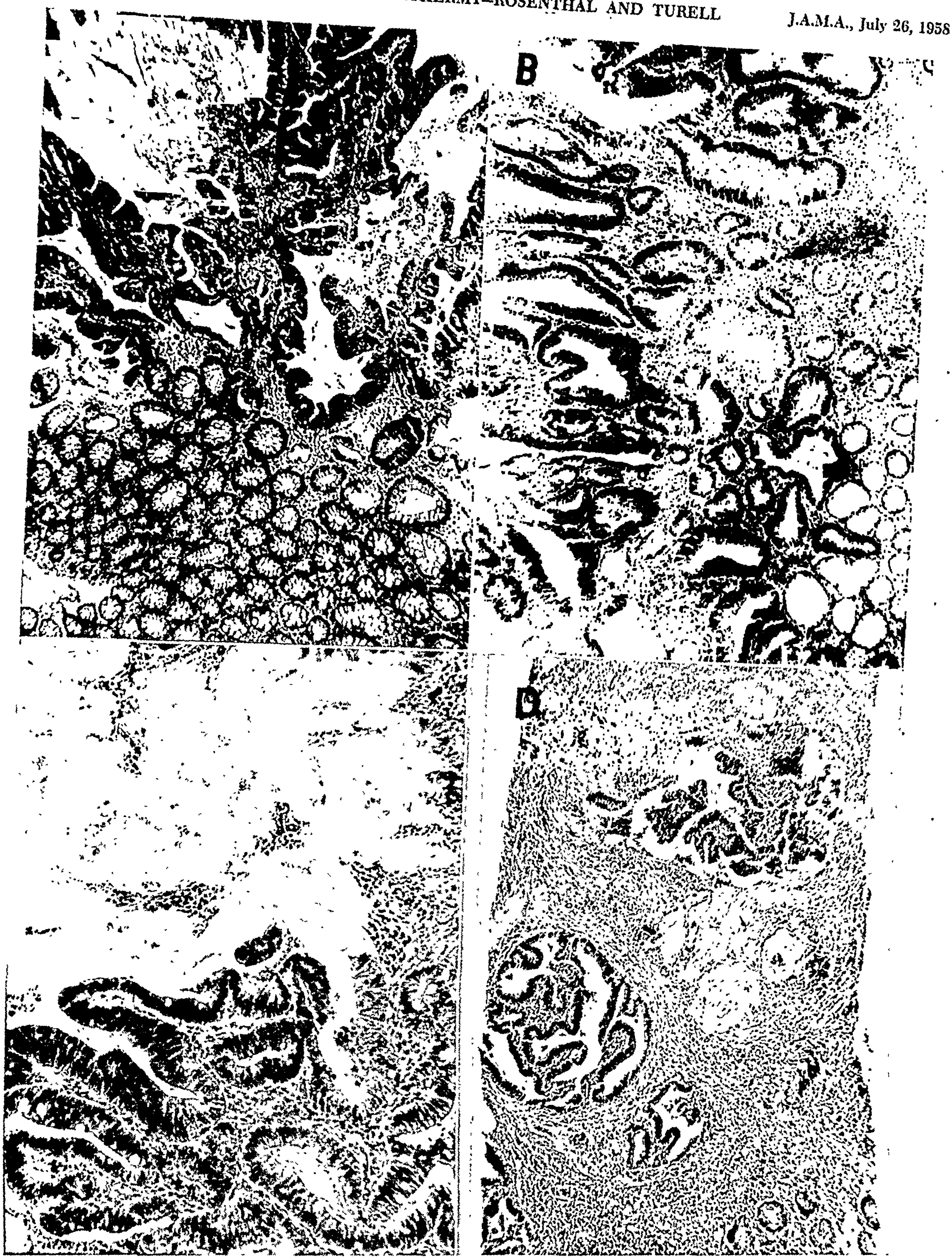

Fig. 2.—*A*, example of very superficial, or implantation, adenocarcinoma of rectum. *B*, more advanced superficial lesion. Note absence of involvement of the muscularis mucosae. *C*, early infiltration of rectal adenocarcinoma as noted in case 2. An essentially similar lesion was present in case 3. *D*, adenocarcinoma with invasion of muscularis mucosae as noted in case 4. (Magnification of *A*, *B*, and *C* is 60× and of *D* 30 ×.)

margin. A roentgenogram of the right humerus revealed a lytic lesion. Biopsy of the osseous lesion disclosed anaplastic carcinoma with a microscopic pattern identical with the malignancy of the bladder. Sigmoidoscopy again revealed normal mucosa at the site of coagulation of the rectal neoplasm. He was discharged on May 25, 1957, and subsequently died at another hospital. Autopsy was not performed.

CASE 4.—A 58-year-old woman (reported on through the courtesy of Dr. Bernard Friedman) was first seen on Sept. 27, 1952, at which time she complained of rectal pain of four to five years' duration. In 1946, she had had an episode of rectal bleeding, and a barium enema at that time revealed a defect of the rectosigmoid which corresponded to the endoscopic finding described below. Therapy was refused. Four months prior to her admission to the hospital she developed increasing constipation and rectal bleeding associated most often with a bowel movement. She was subsequently examined with the sigmoidoscope, a small sessile mucosal elevation 15 cm. above the anal verge was removed with a cold biopsy forceps, and the base was coagulated. Microscopy of the specimen revealed infiltrating adenocarcinoma (fig. 2*D*). Double contrast barium enema and sigmoidoscopy about a fortnight later failed to reveal the site of the biopsy or the presence of any other lesions. Nevertheless, laparotomy was advised, but the patient refused. She was last seen in December, 1957, at which time she was free from gross evidence of rectal malignancy.

In cases 2, 3, and 4 are examples of rectal cancer with infiltration that responded to electrothermia. In cases 2 and 3 it is possible that the infiltration had not extended through the muscularis mucosae, while in case 4 the infiltration appeared to have extended beyond this anatomic structure. This matter could have been resolved by the local excision of the lesion (this patient refused surgical intervention). However, theoretically, we eschew this procedure because it carries potential harm of dissemination of cancer cells and because this procedure still falls short of revealing metastatic involvement of the mesenteric lymph nodes.

For the present, or until more experience is accumulated, we intend to continue to treat infiltrative cancer of the rectum in good-risk patients by the currently accepted surgical procedures. Electrothermic coagulation is reserved for invasive rectal cancer in patients who are extremely poor risks for major operation.[4]

Summary and Conclusions

In view of the reawakening of interest in the treatment of rectal cancer by means of electrocoagulation, this report is concerned with the good results that have been obtained in the treatment of three recent cases of infiltrative adenocarcinoma. At this time we have no uncontested explanation for these good results, particularly in view of the fact that our over-all results with electrothermia for the treatment of similar lesions have been almost universally unfavorable in a series of over 50 unreported cases. Also reported is one favorable result after electrocoagulation of a noninfiltrating (superficial) adenocarcinoma. This good result corresponds to that obtained in 12 other, unreported, followed cases.

For the present, electrothermia is utilized for the treatment of rectal adenocarcinoma in selected cases of poor-risk patients or for the rare person who refuses colostomy. In spite of the occasional apparent but unexplained therapeutic success, electrothermia should be regarded as a palliative procedure for the treatment of invasive cancer of the rectum. For the good-risk patient with invasive rectal cancer, we are continuing to advise accepted surgical procedures as the proper prevailing treatment.

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CARDIAC PACEMAKERS.—Since the advent of open-heart operations, surgical damage to the conduction system during operation has become prevalent. Complete atrioventricular (AV) block cannot always be avoided and has been a factor contributing to mortality, either immediately after the operation or later. Now, complete AV block has become reversible by means of cardiac pacemakers. A cardiac pacemaker provides a rhythmic electric stimulus to the ventricles to increase the ventricular rate. If the stimulus is adequate, the ventricles accept the rhythm imposed by the pacemaker, provided that it is faster than the intrinsic ventricular rhythm. . . . To undertake open-heart operations without a pacemaker at hand no longer seems justifiable.—Frederick Olmsted, W. J. Kolff, M.D., and D. B. Effler, M.D., Electronic Cardiac Pacemaker . . . *Cleveland Clinic Quarterly,* April, 1958.

J.A.M.A., July 26, 1958

COMPLICATIONS FOLLOWING USE OF INDWELLING CATHETERS OF INFERIOR VENA CAVA

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The insertion of a catheter into the inferior vena cava for venoclysis is sometimes a life-saving measure, but it carries a significant degree of risk. In most of the 24 cases here studied the catheter was inserted through a needle into a femoral vein and threaded into the vena cava. Thirteen patients tolerated the indwelling catheter for from 3 to 14 days with no complications. The remaining 11 patients suffered various complications. Four cases are presented in some detail to illustrate the four principal complications encountered: local thrombosis, thrombosis with embolism, suppurative thrombophlebitis with septicemia, and chemical necrosis resulting from the infusion of irritant solutions. The results were fatal in three of these cases. Among the most important contraindications are thrombophlebitis in the lower extremity, infection about the site of insertion of the catheter, and pelvic inflammatory disease. If the use of a caval catheter is indicated, rigid asepsis must be maintained, infusion of solutions known to be irritant or sclerosing action should be avoided, and the flow should be slow and constant rather than intermittent. The caval catheter is a valuable therapeutic tool, but it must be used with due regard to limitations and hazards.

During the past two decades, there has been considerable interest in fluid and electrolyte management, and an increasing number of patients have been salvaged by vigorous and meticulous control of their fluid and electrolyte needs. New techniques have been evolved to overcome the problems which might limit the successful administration of the necessary fluids and solutes. In 1945 Meyers[1] recorded the first use of a plastic (polyethylene) catheter for the introduction of fluids intravenously. This catheter remained in place for up to five days while penicillin and heparin were being administered. The only sequela to this was a local reaction at the site of insertion. Guenther and his associates[2] in 1947 recorded their experience with 18 patients who had had plastic catheters in place intravenously for periods of up to 14 days and listed no complications.

Reports of Experiences with Catheter

Polyethylene has been proved to be a useful plastic material whose presence within tissues evokes little or no inflammatory reaction.[3] There is evidence to demonstrate its value as a flexible plastic material with minimal inflammatory response when placed in living tissues.[4] The bland character of polyethylene is thought to be due to the fact that it has inherent flexibility and elasticity and requires no plasticizer to produce these qualities. The plasticizers are indicted as the tissue irritants in other plastic materials.[5]

Although the use of a flexible, smooth-walled plastic catheter facilitated fluid administration in peripheral veins, local reactions still occurred at the site of the cut-down and required the removal of the catheter and placement into other veins. When intravenous therapy had to be continued over a long period of time, or when markedly hypertonic solutions were being used, a catheter introduced through the femoral vessels into the inferior vena cava became the only practical route of administration. Duffy,[6] in 1949, recorded the first placement of a "femoral catheter" in 28 patients after major surgery. Two of these patients developed phlebitis as noted by increased temperature and by local pain and swelling, but there were no fatalities. Twenty-five cases of inferior vena cava catheterization, with intermittent fluid therapy lasting up to 36 days, were recorded by Ladd and Schreiner[7] in 1951. No clinical cases of thrombophlebitis were recorded, but one patient had transient ischemia of the leg, thought to be due to femoral artery spasm related to the use of the catheter. Autopsy material was available in three patients who had a caval catheter in place for 5, 7, and 36 days, respectively, and in none could a lesion be identified which could be directly related to the use of the catheter. Bonner[8] reported his experience in 41 patients in whom a catheter had been in place in the inferior vena cava for periods ranging from 1 to 131 days. Three patients developed clinical signs of thrombophlebitis, and one of these had a suppurative thrombophlebitis. He also included one patient who had a nonfatal septic pulmonary

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embolus. Autopsy data in 18 cases showed that the caval catheter was not a contributing factor in the cause of death. In no case was there evidence of mural thrombosis in the vessels which had contained the catheter, but five patients showed clot formation about the catheter itself. These cases represent the first documented description of thrombi forming on inlying catheters. Page and Stephens[9] reported the use of a caval catheter in 20 patients who received intermittent fluid therapy for periods ranging from 1 to 50 days. One patient demonstrated clinical thrombosis; nine others who died of their primary disease were examined at autopsy, and three of these showed thrombosis of the vena cava or the iliac veins. Stoberl[10] used polyvinyl tubing for caval catheterization in 87 patients. In his first group of seven patients the catheter was introduced by a cut-down into the femoral vein and thence into the inferior vena cava. These remained in place for varying periods up to a maximum of 14 days with no complications. In the second group, which comprised the remaining 80 cases, the catheter was introduced by a cut-down into the saphenous vein and then threaded cephalad through the femoral vein and into the inferior vena cava. In this group the catheter again was in place for variable periods, with the maximum period being 27 days. Of these 80 patients only 2 showed complications. In a girl aged 7, there was local phlebitis. In a man aged 67 who had had preexisting thrombophlebitis of both lower extremities the autopsy showed thrombosis of the venous channels of the legs, extending into the iliac veins. The catheter itself was encased in a thrombus.

Complications After Use of Catheter

Although previous studies of the use of caval catheters had shown few serious sequelae and no fatalities directly related to the procedure, our experience indicated that there were greater hazards, and it was for this reason that a study of the complications of the use of inferior vena cava catheters was undertaken. The data used in this study were compiled from several hospitals in Seattle.

Twenty-four patients with caval catheterization, representing the total experience at one hospital in Seattle during the period of 1953 to 1956, were available to us for study. At this institution intensive study of fluid and electrolyte therapy was being conducted. Introduction of the catheter in most of these cases was carried out by use of a large caliber-needle puncture of the femoral vein. The catheter was inserted through the needle and threaded into the inferior vena cava, and then the needle was removed. With two patients the cut-down technique was used. Table 1 lists the 13 patients from this group in whom no complications were noted. These patients carried the catheter from 3 to 14 days, with an average of 6 days. The remaining 11 patients exhibited various types of complications: 5 developed mural thrombosis of the inferior vena cava, 2 had thrombosis with pulmonary embolism, and 4 had suppurative thrombosis with septicemia. These patients are listed in table 2 and are grouped in regard to the type of complication. In the group with complications the catheter was in place from 17 hours to 36 days, with an average of 13 days. All patients, whether or not they had complications, received the same type of solutions through the catheter except for the patients in cases 12 and 15, who were given in addition 0.1 *N* hydrochloric acid. In this group of 24 patients, 46% developed complications. All patients included were unselected and received no special care relative to their caval catheter. All patients in this series were severely ill and required intensive and complex fluid and electrolyte therapy. The remaining six patients, marked in table 2, had major complications which were discovered at autopsy at other hospitals. Data from these hospitals are limited to these six cases. We wish to emphasize that this information does not provide an index of the frequency of complications. Four cases, given in more detail, illustrate the four principal complications encountered: local thrombosis, thrombosis with embolism, suppurative thrombophlebitis with septicemia, and chemical necrosis.

TABLE 1.—*Uncomplicated Cases of Inferior Vena Cava Catheterization. Hospital A, 1953-1956**

Case No.	Age and Sex	Underlying Condition	Duration, Days	Infusion Material, % Dextrose in Water	Autopsy
1	48 M	Malignant nephrosclerosis hypertensive cardiovascular disease, low salt syndrome	11	20	Yes
2	46 M	Lower nephron nephrosis, acute hemorrhagic pancreatitis	4	20	Yes
3	64 M	Rheumatic heart disease, with aortic stenosis, mitral stenosis, aortic insufficiency, mitral insufficiency, pulmonary emboli secondary to right auricular thrombosis	3	20	Yes
4	62 M	Carcinoma of stomach, metastases to liver, biliary tract, adrenals	4	50	Yes
5	63 M	Adenocarcinoma rectum; renal shutdown, cause unknown	8	50	No
6	66 M	Essential hypertension	12	5-20	No
7	77 M	Adenocarcinoma, left kidney; arterionephrosclerosis	8	20	No
8	60 M	Arteriosclerotic occlusion of abdominal aorta; acute renal failure secondary to sodium acetrizoate (Urokon) aortogram	10	50	No
9	48 M	Acute renal failure, 2° naphthalene exposure	6	50	...
10	56 M	Multiple myeloma	14	?	...
11	35 M	Perforated abdominal viscus, general peritonitis abscess, left subphrenic and pelvic	5	20	...
12	? M	Hypertensive cardiovascular disease, renal shutdown	5	?	...
13	? M	Hypertension, renal shutdown	10	?	...

* In these cases, catheter was placed with use of large caliber needle puncture

Report of Cases

CASE 1 (local thrombosis).—A 93-year-old male, with hypertensive cardiovascular disease, was admitted because of a cerebrovascular accident. Because of hypernatremia the patient was placed on a fluid balance regimen. Satisfactory peripheral veins could not be found, and hypodermal clysis was an inadequate route for administration of fluids. Therefore, a caval catheter was introduced by needle puncture into the right femoral vein on the third hospital day, and a daily infusion of 2,500 cc. of 20% dextrose in distilled water was given. However, his temperature rose to 104 F (40 C), and he became less responsive and died on the 10th hospital day. The caval catheter had been in place for seven days. The final impression was hypertensive cardiovascular disease, with a recent cerebrovascular accident.

At autopsy, the right common iliac vein contained a plastic catheter doubled on itself, and this was surrounded by a thrombus adherent to the wall in several places (figs. 1 and 2). The catheter extended into the ileolumbar tributary behind the right psoas muscle. In addition to this, there was evidence of severe coronary arteriosclerosis with some myocardial fibrosis. A small fresh myocardial infarction was noted at the apex. Thrombosis of the inferior carotid artery was also present, and the right cerebral hemisphere had undergone massive infarction.

TABLE 2.—*Complications Following Inferior Vena Cava Catheterization: 1953-1956**

Case No.	Age and Sex	Placement Method†	Underlying Condition	Duration, Days	Infusion Material, % Dextrose in Water	Complications to Catheter‡
1	93 M	N	Thrombosis (right internal carotid artery); myocardial infarction, old and recent	7	20	T—Catheter doubled up in right common iliac vein, surrounded by recent thrombus adherent to wall in several areas.
2	48 M	N	Cirrhosis with ascites; bleeding esophageal varices	4	50	T—Surrounding catheter in inferior vena cava and attaching it to wall. Thrombus in left femoral vein.
3	44 M	CD	Malignant arteriolonephrosclerosis; cardiorespiratory failure	2	20	T—1-cm. thrombus on posterior wall of proximal femoral vein; 0.5-cm. attached thrombus in middle femoral vein.
4	39 M	N	Acute exacerbation of glomerulonephritis; pulmonry edema; bronchopneumonia	36	50	T—Several small thrombi around tubing and attached to wall.
5	56 M	N	Portal cirrhosis, esophageal varices	16	50	T—Antemortem thrombi surrounding catheter. Long linear thrombus 0.5 cm. in diameter extending 6-7 cm. along wall of inferior vena cava; final 2-3 cm. not attached.
6§	18 F	N	Acute renal failure; ileocutaneous fistula; hepatic failure	15	50	T—Catheter coated with fibrinous material 0.4 cm. in diameter; degenerating cellular elements.
7§	4 M	CD	Renal failure due to bismuth intoxication	13	50 5% ethyl alcohol, whole blood	T—Thrombosis of inferior vena cava and left common iliac vein, adherent to wall.
8§	3 M	CD	Anuria, acute glomerulonephritis	6	50 5% ethyl alcohol	T—Thrombosis of left common iliac vein.
9	60 M	N	Cerebral arteriosclerosis with massive infarction	37 (changed at 30)	20	TPS—Left common iliac vein—pyemia with multiple widespread abscesses.
10	55 M	N	Portal cirrhosis, esophageal varices, hepatic failure	5	20	TPS—Several large abscesses in right inguinal area. Metastatic abscesses of epicardium.
11	66 M	N	Reticular cell sarcoma in hilar region of lung, stomach	15	20-50	TPS—No autopsy. Area infected, blood culture positive for β hemolytic Staph. pyogenes.
12	48 M	N	Hepatic coma secondary to liver cirrhosis	17 hours	2 liters of 10, with 0.1 **N** HCl	TPS—Suppurative TP of right common iliac vein.
13§	45 M	CD	Common duct stone; postoperative jaundice	7	20	TPS—Right saphenous vein, blood culture positive for Staph. pyogenes var. aureus.
14§	45 F	N	Ulcerative colitis, severe malnutrition, skin abscesses, thrombophlebitis opposite leg	10	20	Septicemia—no residual thrombus at autopsy.
15	53 M	N	Liver cirrhosis, with hepatic coma	7	10 with 0.1 **N** HCl	TE—Endophlebitis with thrombosis of inferior vena cava and right common iliac vein. Multiple pulmonary emboli in right lung.
16	62 M	N	Gastrocolic fistula secondary to gastrectomy. Duodenal pancreatic fistula	7	10	TE—Inferior vena cava thrombus to right common iliac vein. Bilateral pulmonary emboli, with massive infarction of lower lobes.
17§	40 M	N	Diabetes mellitus and postinsulin shock, ventricular fibrillation	12	5-10	TE—Thrombosis of left femoral and hypogastric veins. Embolus right pulmonary artery.

* Autopsy was performed in all but case 11.
† N = needle; CD = cut-down.
‡ T = thrombosis; TE = thrombosis with embolus; TPS = thrombophlebitis with suppuration and/or septicemia.
§ Cases from hospital other than Hospital A.

The complication here consisted of a local thrombosis which had no clinical manifestations. If the patient had recovered this might well have been an entirely silent episode. Death was due to a cerebrovascular accident plus his underlying cardiovascular disease.

CASE 16 (thrombosis followed by fatal pulmonary embolus).—A 62-year-old male had a wound disruption and multiple fistulas after gastric resection for duodenal ulcer. He was maintained with jejunostomy feedings, and fluids were given intravenously to correct his electrolyte imbalance. A caval catheter was inserted through the right femoral vein on the second hospital day, and 2 liters of 10% dextrose in water was given daily as well as three blood transfusions. The patient's condition improved until the sixth hospital day, when he suddenly developed generalized pain, cyanosis, and shock. Despite the use of oxygen and vasopressors he rapidly developed abdominal distention and an ileus. Peritoneal puncture revealed thick, purulent material. In spite of transfusions and supportive care he died 48 hours later.

At autopsy, in the inferior vena cava, just below the junction with the renal veins, there was an adherent plaque of thrombotic material extending down into the right iliac vein. Straddling the bifurcation of the pulmonary artery was a large embolus showing mild adherence to the wall and involving several branches of the pulmonary artery. A smaller coil projected into the left branch. A Billroth 2 gastrectomy, with a retrocolic gastrojejunostomy, was present. There was perforation of the anastomosis, with formation of multiple fistulas and purulent peritonitis. Microscopic examination showed the thrombus in the right common iliac vein to have undergone some organization at its base.

This is an example of thrombosis which was no longer localized but which had been a source of massive pulmonary embolus, a direct cause of death in this individual. The patient was extremely ill, of course, and might well have died from his underlying illness.

Case 13 (thrombophlebitis followed by septicemia).—A 64-year-old man was admitted with long-standing obstructive jaundice, persisting despite removal of a common duct stone. In addition to jaundice, the patient was found to have marked nitrogen retention and dehydration. It was decided to reexplore the patient, and in order to prepare him as rapidly as possible for surgery it was decided to use a caval catheter introduced by way of the saphenous vein. Five days later, the temperature rose to 101 F (38.3 C), and the fever persisted. The cause of the fever was not apparent until examination of the cut-down site indicated a wound infection. About 1 oz. of pus and hemolyzed blood was obtained on opening the cut-down site, and coagulase culture was positive for hemolytic Staphylococcus pyogenes var. aureus. The patient's subsequent course was progressively downhill, with persistent fever, decreased urinary output, and a positive blood culture for the same staphylococcic organism.

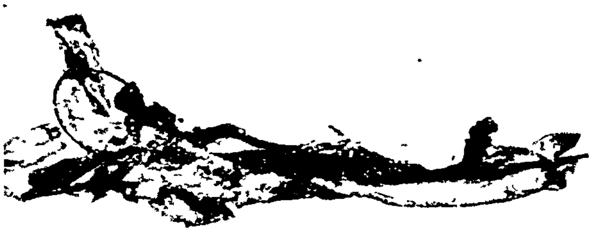

Fig. 1 (case 1).—External and common iliac vein, showing extensive but localized thrombosis involving catheter. (Scale is in centimeters.)

At autopsy there was evidence of septicemia, with metastatic abscesses encountered in lungs, spleen, and kidneys. The common duct was normal in caliber at this time and showed no obstruction. The cut-down incision in the right inguinal area showed the saphenous vein to be partially thrombosed and to contain purulent material. This suppurative thrombophlebitis extended for a distance of about 4 cm. (fig. 3).

The underlying problem here consisted of severe hepatic damage due to long-standing obstructive jaundice with terminal biliary nephrosis. The complication following the use of the caval catheter was a serious one consisting of suppurative thrombophlebitis, which eventually resulted in septicemia, with establishment of abscesses in numerous other major viscera. The indication for the use of the catheter in this individual consisted only of the desire to prepare him more rapidly for operation.

Case 15 (chemical necrosis).—A 53-year-old male, with long-standing cirrhosis, was admitted with impending hepatic coma. Treatment consisted of bed rest and 10% dextrose solution with vitamins given intravenously. There was little response, and the patient's carbon dioxide level fell to 16 mEq. per liter; the blood pH was 7.55, and respirations were deep and rapid. A caval catheter was placed percutaneously by needle. During the next five days, 9 liters of 10% dextrose solution containing 0.1 *N* hydrochloric acid were given. He became more responsive and was able to answer questions fairly rationally. However, at this time he became hyperpneic and there was bleeding from the mouth, around the catheter, and from the rectum. The clotting time was eight minutes, the bleeding time two and one-half minutes, and the hematocrit 39%. Protamine sulfate and vitamin K were administered. He remained dyspneic and finally died.

At autopsy the inferior vena cava showed a granular intima to which were adherent old, as well as relatively recent, friable red-grey thrombi. These did not occlude but were adherent over broad areas of intimal surface in association with the catheter, which extended into the inferior vena cava for a distance of about 5 cm. The right iliac vein was also affected, and there were thrombi adherent both to the catheter and to the intima. Additional gross findings at autopsy consisted of numerous pulmonary emboli in the right lung, with multiple petechial hemorrhages in the central nervous system and two small areas of encephalomalacia. There was a severe portal cirrhosis and chronic pyelonephritis. Microscopic study showed a wide zone of coagulation necrosis and unorganized antemortem thrombotic material within the lumen of the inferior vena cava. There was widespread chronic inflammation, numerous cells, and many foci of hemorrhage (fig. 4).

This complication consisting of a chemical necrosis of the wall of a vein is probably due to the use of irritating materials through the catheter rather than due to the presence of the catheter itself. It does represent one type of complication, however, which can be encountered through use of the caval catheter. This thrombosis was not entirely confined to the vein and undoubtedly was the origin for the small pulmonic emboli which were noted.

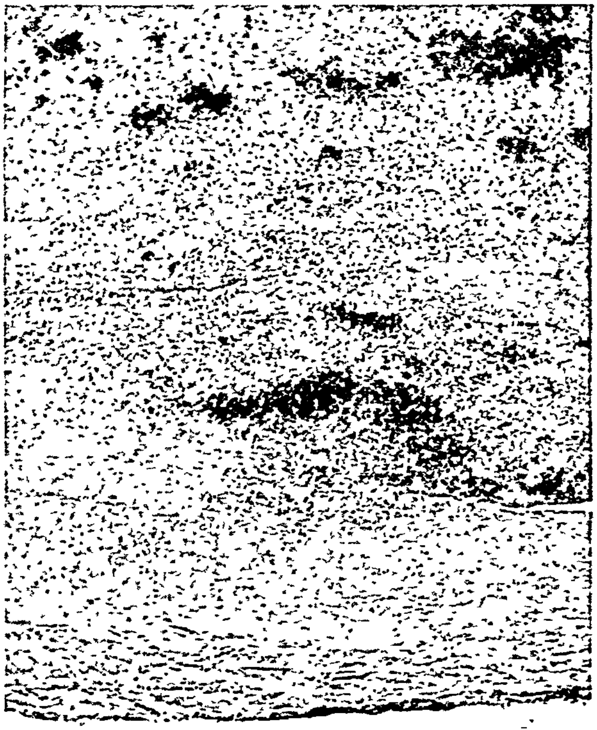

Fig. 2 (case 1).—Common iliac vein, showing attachment of thrombus to intima and well-defined architecture of thrombus. Hematoxylin-eosin stain (× 60).

Comment

The use of indwelling caval catheters is recognized as a necessary technique in therapy, and the complications tabulated in this study should not produce the impression of discrediting this valuable tool. However, as with most effective devices, there are limitations and hazards in its use, and there seems to be either a lack of recognition of this or at least some confusion as to the degree of hazard.

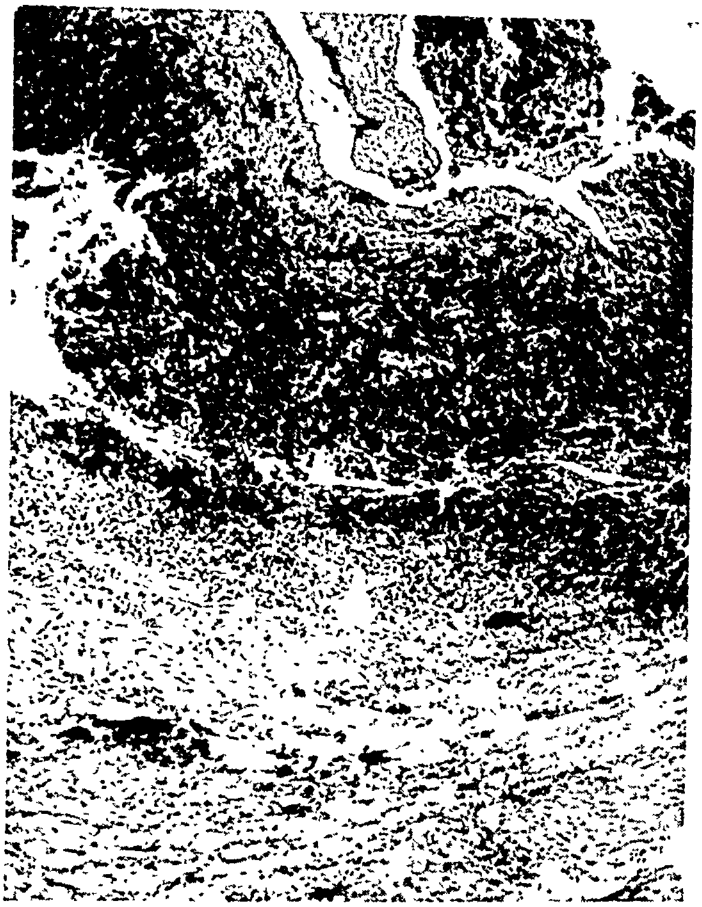

Fig. 3 (case 13).—Saphenous vein with suppurative thrombophlebitis. Hematoxylin-eosin stain (× 60).

Four cases are listed in our series in which complications due to the caval catheterization can be considered the cause of death (cases 10, 13, 16, and 17). The most common complication is thrombosis, and it may remain a localized problem without systemic complication. Fatal pulmonary embolism, however, may occur, and the development of even localized thrombi in a vein without valves, such as the vena cava, constitutes a serious problem because of the ease of dislodgment of such thrombi into the pulmonary circulation. The complication of infection is serious and frequently results in bacteremia with systemic manifestations. Although in this group there is a relatively high percentage of complications and fatalities, it should be emphasized that all these patients were severely ill and that the underlying illness could have contributed to the type and extent of the complications. Another possible explanation of the apparently high percentage of complications could be the fact that autopsy data were available on most patients who died and that a specific search for complications due to the use of the catheter was made.

Several mechanisms can be considered as partially responsible for clot formation within the veins containing catheters. Undoubtedly the most important is mechanical trauma to the intima, either during placement of the catheter or by movement within the vascular stream. Clotting is initiated by release of thromboplastin from injured tissue and especially the intima. The second factor is chemical trauma. Jones[11] in 1954 pointed out that thrombi formed primarily at the catheter tip and not at the point of entry into the vein, suggesting that the infusion of fluid itself acted as an irritant. Certainly hypertonic dextrose solution and especially 0.1 *N* hydrochloric acid are recognized sclerosing agents. The polyethylene catheter itself, however, does represent a foreign substance and, despite its minimal tissue reaction, also constitutes a source for stimulating thrombosis. Lastly, thromboses are more prone to develop in a slow venous stream, and the length of time a catheter remains in place must be recognized as a factor in the development of clotting. This is illustrated by the fact that in the patients showing complications an average of 13 days' use of a catheter was found, whereas in patients without complications the average time of use had been only 6 days. An effort was made to relate the data available on

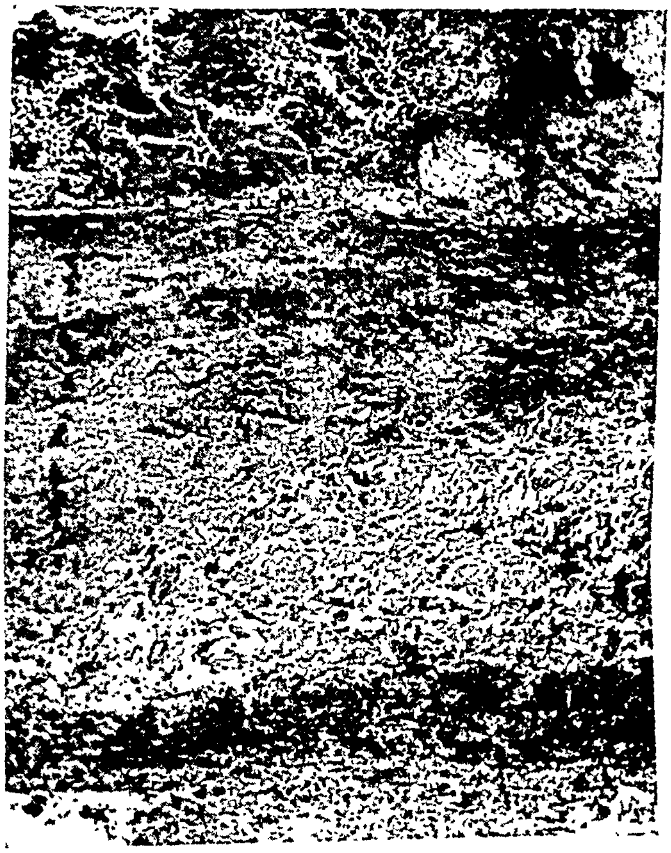

Fig. 4 (case 15).—Inferior vena cava. There is chemical necrosis of vein wall, with mural thrombosis. Hematoxylin-eosin stain (× 60).

coagulation studies in these patients to the formation of thrombi. These studies included, in some instances, prothrombin times, clotting times, and platelet counts. However, there did not seem to be any significant alteration in these measurements to explain the formation of thrombi. Since most of the primary clotting factors are present in the blood, much in excess of the minimal physiological requirements, changes in concentration over a wide range probably do not alter the coagulation of blood.[12]

The inferior vena cava catheter, although an effective therapeutic tool, carries a significant degree of risk. Peripheral veins should be used first even when such markedly hypertonic solutions as 50% dextrose are required. The caval catheter should be employed only when peripheral veins are exhausted. A possible exception is in children, when rapid transfusions or infusions are required and the peripheral vessels cannot accept the necessary rate of flow. The most important false indication is the use of the caval catheter to escape the necessity of supplying adequate nursing supervision or to avoid annoyance to the house staff. Rapid preparation of the patient for surgery or the necessity for avoidance of peripheral thrombophlebitis due to needle puncture are not valid indications for use of a caval catheter.

There are other recognizable situations in which the use of a caval catheter should be deliberately avoided. It should not be used for patients with lower extremity thrombophlebitis, local infection at the site of the catheter entrance, and pelvic inflammatory disease. In patients showing thrombogenic diatheses, such as those with congestive failure, polycythemia, prolonged hypertension, and thrombocytosis, one must balance the need of the catheter against the increased hazard. Whether the use of a trocar or introduction through a cut-down is safer remains a moot question. In either instance the need for rigid asepsis must be stressed. Continuous flow would seem to be advisable rather than intermittent use because it avoids the formation of a clot within the lumen of the catheter, allows the fluid to be diluted to the maximal extent, and permits the maximum amount of calories to be used, as well as avoiding wastage of glucose and amino acids in the urine.[13]

Summary

The inferior vena cava catheter is a result of ingenuity and persistence in finding a means of supplying fluids and electrolytes in patients who have no remaining accessible venous channels. The technique has proved attractive because of the ease of management and because of reduction in care on the part of the nursing personnel and house staff.

Complications attending the use of the indwelling caval catheters employed for intravenous therapy in a series of patients observed over a four-year period included local thrombosis, thrombosis with embolism, suppurative thrombophlebitis with septicemia, and chemical necrosis. In a group of patients surveyed at one hospital during this time, a 46% incidence of complications was observed as demonstrated by autopsy findings. Four deaths were ascribed directly to complications following use of an indwelling caval catheter. The employment of this therapeutic tool is recognized as important in many instances, but attention is directed to contraindications and hazards which may arise.

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UNCOATED BUFFERED FERROUS SULFATE

ABSORPTION IN MAN OF RADIOACTIVE IRON (FE^{59}) AS FERROUS SULFATE MEASURED ELECTRONICALLY

Alison H. Price, M.D., Lowell Erf,† M.D.
and
James Bierly, M.S., Philadelphia

A radioactive isotope of iron was administered to 10 patients by mouth in order that its absorption into the blood might be studied. Each dose consisted of 10 cc. of an aqueous suspension containing 0.1 mc. of $Fe^{59}SO_4$ with 200 mg. of stable ferrous sulfate and 200 mg. of magnesium aluminum hydroxide. The appearance of the isotope in the blood was manifested by a rise in the radioactive disintegration count from an average of 265 counts per minute per 5 cc. sample to figures as high as 582. Counts were made on the whole blood because the serum alone showed very little radioactivity. The daily administration of two uncoated tablets, each containing 200 mg. of ferrous sulfate and 200 mg. of magnesium aluminum hydroxide, was carried out in 27 patients, all of whom had reported nausea and other gastrointestinal symptoms after taking other iron preparations in unspecified doses. In this series no patient experienced nausea, and there was but one case each of diarrhea and abdominal cramps. The presence of the buffer did not prevent the absorption of iron even when the total acidity of the gastric juice was extremely low. The absence of a coating on the tablets was believed to favor early absorption.

It is generally accepted that ferrous sulfate is the most efficacious form of orally given iron (Goodman and Gilman,[1] Moore and Dubach,[2] and Hahn and others[3]). A report to the Council on Foods and Nutrition,[4] in 1956, stated, "The human absorbs iron mostly, if not entirely, in its ferrous form." However, the incidence of adverse reactions to iron medication is high. These conditions led to the development of uncoated ferrous sulfate tablets buffered with magnesium aluminum hydroxide (Fermalox). Each uncoated tablet contains 200 mg. of ferrous sulfate, buffered with 200 mg. of magnesium aluminum hydroxide.

We have demonstrated that, when this preparation is tagged with radioactive iron (Fe^{59}), the buffered ferrous sulfate is effectively absorbed in proportion to the needs of the body. With continued use, a satisfactory rise in reticulocyte and hemoglobin levels has also been shown. Furthermore, there has been practically complete absence of adverse reactions in patients known to be intolerant of other iron medicaments.

Absorption Determined by Radioactive Iron (Fe^{59}) Tracer

The use of a radioactive tracer furnishes the best means of determining the absorption and further fate of administered iron.[5] This method was employed in a series of 10 cases with use of the uncoated buffered ferrous sulfate tablets. Each patient was given by mouth 0.1 mc. of Fe^{59} as ferrous sulfate, intimately mixed with 1 Fermalox tablet in a 10-cc. suspension.

Venous blood was taken at ½, 2, and 24 hours, and the counts were compared with the background readings. Counts were made on whole blood because, in our experience, the serum, when tested, showed very little radioactivity. The uptake of iron in this series of patients is shown in table 1.

It will be noted that there was a substantial uptake of iron in all patients except that in case 3. This patient was moribund, with metastatic carcinoma of the pancreas. The absence of a positive reading in this case tends to confirm the accuracy of the test. The following comment is offered with respect to the results recorded in table 1.

Case 1.—In this patient, there was substantial absorption of iron in spite of achlorhydria and extremely low total acidity of the gastric juice.

Case 2.—Iron absorption is active in polycythemia, a condition in which there is seldom a physiological need for iron. The results in this patient might be considered as a control for the upper limit of absorption.

Case 3.—There was no absorption of iron in this moribund patient with metastatic carcinoma of the pancreas, which confirmed the accuracy of the test. It is well known that the absorption of iron from the intestinal tract is negligible in severe infections and in terminal states.

Case 4.—Subtotal gastrectomy for duodenal ulcer was performed 18 hours after administration of the iron, that is, 6 hours before the last count was made. The sharp fall in the 24-hour count signifies a marked upheaval in iron metabolism during and after the trauma of surgery and anesthesia.

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CASE 5.—This patient with a fractured rib had adequate iron absorption, which was not upset by the acute trauma to the chest and abdomen.

CASE 6.—Results in this patient with hereditary leptocytosis apparently confirm the fact that absorption of iron from the intestinal tract is not influenced by recent intravenous injections of iron.

CASE 7.—Findings in this patient with periarteritis nodosa show a very high uptake of iron well maintained over the 24-hour period.

CASE 8.—The initial increase in this patient with purpura was not maintained in the 2-hour and 24-hour counts. A possible explanation is quick storage of the absorbed iron.

CASE 9.—Severe hypothyroidism with an extremely low basal metabolic rate did not interfere with adequate absorption of iron in this patient, but the last two counts could be interpreted as showing slower storage.

CASE 10.—This patient with duodenal ulcer showed excellent uptake even though clinically there was no apparent bleeding.

Absorption of Iron from Duodenum

With use of a radioactive tracer in dogs, Hahn and others[6] established that approximately 90% of iron absorption occurs in the duodenum. As shown in table 1, Fermalox tagged with Fe^{59} is effectively absorbed within one-half hour after administration. This result confirms the observations of Moore and Dubach[2] to the effect that the usual therapeutic dose of an antacid does not affect the absorption of iron.

TABLE 1.—*Iron Uptake in Whole Blood Determined After One Uncoated Buffered Ferrous Sulfate Tablet Mixed with Fe^{59} Was Taken*

					Counts/Min/5 Cc				
Case No	Sex	Age, Yr	Diagnosis	Date	Background	½ Hr	2 Hr	24 Hr	Remarks
1	F	48	Neuritis	9/20/54	293	435	356	391	Achlorhydria
2	M	52	Polycythemia	12/ 2/54	231	405	395	552	RBC 7 million/cu mm.
3	M	56	Terminal cancer	12/ 2/54	252	236	263	258	Died 8 days later
4	F	61	Duodenal ulcer	12/17/54	259	410	553	348	Subtotal gastrectomy 6 hr before final reading
5	F	24	Fractured rib	12/17/54	264	509	556	410	Test same day as injury
6	F	40	Hereditary leptocytosis	12/20/54	287	440	405	386	2 recent intravenous iron injection[a]
7	F	47	Periarteritis nodosa	12/20/54	292	589	495	493	Highest uptake of group
8	F	29	Purpura	12/20/54	233	320	268	244	Splenectomy 9 days previously
9	F	55	Hypothyroidism	12/20/54	275	417	423	405	Basal metabolic rate, −27%
10	M	31	Duodenal ulcer	12/22/54	260	522	501	453	No clinically apparent bleeding
Ave	....	....			265	428	412	397	

The Pharmacopeia of the United States[7] recommends a dosage of 300 mg. of ferrous sulfate three times a day as a hematinic (a total of 900 mg. per day). Since ferrous sulfate contains 20% iron[8] and the utilization rate is given as 15.7%,[9] the daily uptake of iron from this source would be estimated at 28 mg. The minimum adult daily requirement of iron is 10 mg.

In our studies, we have found satisfactory hematopoietic response to a dosage of 2 Fermalox tablets daily, each containing 200 mg. of ferrous sulfate (a total of 400 mg.). This is less than half the above-mentioned dosage of conventional ferrous sulfate. This reduced amount of iron, plus the buffering with magnesium aluminum hydroxide, accounts in large part for the almost complete absence of adverse reactions when ferrous sulfate is administered in the form of Fermalox.

The high utilization rate of iron supplied by uncoated Fermalox tablets is readily explained by their rapid disintegration in the stomach, which makes the iron immediately available for absorption in the stomach and duodenum.

Elimination of Adverse Reactions

Gastric distress, colicky pains, and diarrhea due to ordinary ferrous sulfate are of common occurrence (Goodman and Gilman[1]). Their incidence may interfere with the full dosage required to restore normal hemoglobin levels. In our studies of iron therapy, we have rarely observed any adverse reactions to Fermalox other than an occasional instance of constipation; one patient developed diarrhea. As with all iron medicaments, the stools become black due to formation of iron sulfide.

As shown in table 2, we treated with Fermalox a series of 27 patients known to be intolerant of iron. Of this group, 100% suffered from nausea after receiving other iron medicaments, 89% from burning sensation, 89% from abdominal cramps, and 78% from diarrhea. In this series, there was not a single complaint of nausea or burning sensation due to the Fermalox and only one patient had diarrhea and one had abdominal cramps.

Comment

Iron salts for medicinal purposes are coated, primarily, to prevent oxidation of the ferrous salt to the ferric form and, secondarily, when possible, to prevent gastric irritation. Therefore, the development of a buffered ferrous sulfate preparation which is nonirritating to the upper gastrointestinal tract and which also contains an antioxidant to check the change from the ferrous to the ferric form is of great clinical value.

A less irritating, more easily tolerated medicinal iron compound (Fermalox) fills an important need in the treatment of iron deficiency states. The demonstration of effective absorption by means of the radioactive iron tracer, plus thousands of clinical cases showing satisfactory rise of hemoglobin level, fully establishes the efficacy of this medicament. In addition, the almost complete absence of the common adverse reactions to ordinary iron medicaments enables the physician to continue use of the drug until a satisfactory therapeutic result is obtained.

With reference to the utilization of iron, Sollmann[10] says that isotope studies show that the body absorbs or rejects ingested iron according to its needs. This is in accordance with our experience, as exemplified by table 1, except for the patient in case 2, who had polycythemia.

In case 4, the condition was diagnosed as duodenal ulcer with the likelihood of considerable previous blood losses. The hemoglobin level was 62%; the erythrocyte count was 3,350,000 per cubic millimeter. The Fe^{59} test showed an iron uptake from a background of 259 counts per minute to 410 in one-half hour and 553 in two hours.

Moore and Dubach[2] reported in 1956: "Patients with iron deficiency or hypochromic anemia absorb inorganic iron more efficiently than do normal persons." Hahn and others[3] found that, in a series of nine human subjects to whom iron tagged with radioactive isotope was administered, the ferrous iron salt was much more readily absorbed and subsequently utilized than the corresponding ferric salt or ferric ammonium citrate.

In our experience, rapid rises of reticulocyte and hemoglobin levels follow the use of Fermalox in iron deficiency states following blood losses due to pregnancy, menorrhagia, peptic ulcers, bleeding hemorrhoids, severe injuries, and excessive blood donations.

The utilization of organic iron compounds is known to be incomplete. "Contrary to the older a priori concepts of Bunge and others," writes Sollmann,[9] "it has been definitely established that 'organic' iron compounds are poorly absorbed and that only ionized or ionizable compounds are sufficiently absorbed to be therapeutically effective."

Organic iron must be broken down to the inorganic state before it can be absorbed. It is also known, as Hahn has shown,[11] that the iron in food, animal and vegetable, is largely of the poorly absorbed heme type and that phosphate, phylate, and other dietary ingredients interfere with its absorption. The use of Fe^{59} as a tracer, intimately mixed with the food or medicinal iron to be tested, has fully established that inorganic iron (espe-

TABLE 2.—*Comparison of Adverse Reactions to Buffered Ferrous Sulfate and to Previous Iron Medicament*

				Ferrous Sulfate				Buffered Ferrous Sulfate				
Case No.	Sex	Age, Yr.	Diagnosis	Nausea	Burning Sensation	Diarrhea	Abdominal Cramps	Nausea	Burning Sensation	Diarrhea	Abdominal Cramps	Remarks
1	F	32	Hereditary leptocytosis	+	+	+	+	—	—	—	—	Severe constipation with previous medication; none with latter
2	F	68	Pernicious anemia	+	+	+	+	—	—	—	—	Iron deficiency
3	F	60	Hypochromic microcytic anemia	+	—	—	+	—	—	—	—	Hemoglobin, 71%; RBC 3,720,000/cu. mm.
4	F	51	Hypochromic microcytic anemia	+	—	—	+	—	—	—	—	Hemoglobin, 78%; RBC 4,300,000/cu. mm.
5	F	43	Hypochromic anemia	+	+	+	+	—	—	—	—	Due to severe menorrhagia
6	F	37	Uterine fibroids	+	+	—	—	—	—	—	—	Menorrhagia
7	F	28	Hypochromic anemia	+	+	+	+	—	—	—	—	Hemoglobin, 55%; RBC 2,320,000/cu. mm.
8	M	61	Lymphatic leukemia	+	+	+	+	—	—	—	—	Hemoglobin, 91%; RBC 4,300,000/cu. mm.
9	F	59	Carcinoma of intestine	+	+	+	+	—	—	—	—	Less than ⅓ of her g.i. tract left after operation
10	F	27	Hodgkin's disease	+	+	+	+	—	—	—	—	Menorrhagia; hemoglobin, 52%
11	F	51	Migraine	+	+	+	+	—	—	—	+	Irritable bowel syndrome; tablets caused constipation
12	M	44	Hodgkin's disease	+	+	—	—	—	—	—	—	Hemoglobin, 78%; RBC 4,000,000/cu. mm.
13	F	36	Follicular lymphoblastoma	+	+	+	+	—	—	—	—	Hemoglobin, 65%; RBC 3,400,000/cu. mm.
14	M	17	Chondrosarcoma	+	+	+	+	—	—	—	—	Died in 7 months
15	F	61	Mucous colitis	+	+	+	+	—	—	—	—	Hemoglobin, 75%; RBC 3,800,000/cu. mm.
16	F	62	Follicular lymphoblastoma	+	+	+	+	—	—	—	—	Hemoglobin, 81%; RBC 4,000,000/cu. mm.
17	F	57	Hypotension, hypothyroidism	+	+	+	+	—	—	—	—	Hemoglobin, 71%; RBC 3,600,000/cu. mm.
18	M	51	Myeloid leukemia	+	+	—	—	—	—	—	—	Hemoglobin, 58%; RBC 3,200,000/cu. mm.
19	F	55	Diabetes mellitus	+	—	—	+	—	—	—	—	Hypertension; arteriosclerosis
20	F	63	Myelofibrosis	+	+	+	+	—	—	—	—	Hemoglobin, 43%; RBC 2,400,000/cu. mm.
21	M	35	Hodgkin's disease	+	+	+	+	—	—	—	—	Hemoglobin, 52%; RBC 2,670,000/cu. mm.; died after 8 weeks
22	M	62	Hypochromic anemia	+	+	+	+	—	—	+	—	Hemoglobin, 46%; RBC 2,300,000/cu. mm.
23	F	36	Secondary anemia	+	+	+	+	—	—	—	—	Due to hemorrhoids and fibroids
24	M	52	Hypochromic microcytic anemia	+	+	+	+	—	—	—	—	Chronic prostatitis
25	F	40	Hypochromic microcytic anemia	+	+	+	+	—	—	—	—	Hypothyroidism
26	F	41	Hypochromic anemia	+	+	+	+	—	—	—	—	Hemoglobin, 87%; RBC 4,300,000/cu. mm.
27	F	33	Lupus erythematosus	+	+	+	+	—	—	—	—	Hemoglobin, 71%; RBC 3,400,000/cu. mm.
Total				27	24	21	24	0	0	1	1	

cially ferrous sulfate) is readily incorporated first into ferritin and then hemoglobin after absorption from the upper intestinal tract of man.

Work to date would signify that with food iron the optimal absorption occurs only in the presence of normal gastric acidity. Moore and Dubach[2] found that, in most instances, absorption of Fe ^{59}-tagged food iron is less than 10% in healthy human subjects.

With administration of Fermalox, on the other hand, it was found that there was a good iron uptake when the need existed regardless of gastric acidity. Thus in case 1 (table 1) there was complete achlorhydria with extremely low total gastric acidity. Yet the Fe ^{59} test showed an iron uptake from a background of 293 counts per minute to 435 in one-half hour. This result is contrary to the general belief that normal gastric acidity is needed when iron salts are given orally.

Our findings confirm the general belief that absorption of iron is deficient in severe infections, post-traumatic conditions, and terminal states. As shown in table 1, there was no iron uptake in the patient in case 3, who was moribund with metastatic carcinoma of the pancreas, and in that in case 4 it fell off sharply after the operation of subtotal gastrectomy.

Summary

Buffered ferrous sulfate in uncoated tablets (Fermalox) has a high absorption index, as determined by use of radioactive iron (Fe ^{59}) as a tracer. Reticulocyte and hemoglobin response to buffered ferrous sulfate is highly satisfactory. When this preparation is prescribed, clinical response is obtained with 44% of the dosage of ferrous sulfate recommended by the Pharmacopeia of the United States. The adverse reactions of nausea, burning sensations, diarrhea, and abdominal cramps are almost completely avoided by use of buffered ferrous sulfate.

The Fermalox buffer, magnesium aluminum hydroxide, being adsorbent as well as slightly alkaline, tends to adsorb the phosphorus complexes which interfere with full utilization of ferrous sulfate. The use of an uncoated, rapidly disintegrating tablet allows the acid gastric juice to work advantageously for the utilization of the ferrous sulfate. The uncoated Fermalox tablet is readily broken down, freeing ferrous ions and making them readily available in the first portion of the duodenum, where the most active absorption of iron takes place. Thus, in our opinion, buffered ferrous sulfate in uncoated tablets is the best all-around medicament for use in iron deficiency states.

1618 Locust St. (3) (Dr. Price).

The Fermalox tablets used in this study were supplied by William H. Rorer, Inc., Philadelphia.

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HOSPITALIZATION OF PSYCHIATRIC PATIENTS.—Study and reflection soon provide ample evidence and conviction that removal of the patient from his home and surroundings to a hospital bed—while it may . . . relieve the community of immediate pressures and . . . bring . . . useful treatment routines to bear upon the patient's illness—is by no means an unmixed blessing. For one thing, it may cause the community to postpone indefinitely the development of other more effective treatment facilities and, for another, it may add additional complexities to the patient's own treatment problem. The end point of any psychiatric treatment program is resocialization of the patient and his reintegration with family, with friends, and with industry. Such resocialization comprehends the idea that a released patient's economic and cultural needs will be met, that he will be useful so far as he is physically able, and that his sense of personal worth and dignity will be sustained.—P. E. Feldman, M.D., Psychiatric Hospitalization, *Journal of the Kansas Medical Society,* June, 1958.

EDUCATION AND INSTRUCTION OF PATIENTS IN PRIVATE PRACTICE

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It is necessary that the instructions given to a patient be systematic and complete if intelligent cooperation is to be expected. This is especially true of surgical patients and their families. Whenever possible a separate room should be allocated for this purpose. It should be equipped with comfortable chairs for the patient and for responsible relatives. Chalk board, anatomic models, printed material, a viewing-box for roentgenograms, and facilities for showing parts removed at operation can be extremely helpful. Directions given orally for nursing care, special diets, and the use of drugs or apparatus at home are too easily misunderstood or forgotten; instead, such directions can be put on paper by using standard duplicating equipment. They save countless hours of the physician's time. Attention to this aspect of the physician-patient relationship helps to secure better therapeutic results and to improve public relations.

A planned program for the education and instruction of patients may serve as a valuable adjunct to private practice. The modern patient has been thoroughly indoctrinated in health matters through schooling and modern communications. He expects a detailed and intelligent explanation of his medical problem. Treatment may be rendered more effective if the patient is thoroughly instructed in what to do to help himself. An educational program is especially important in private practice, since a majority of office patients are managed by conservative measures at home. The patient who understands his problem is usually satisfied with his physician, and thus an organized educational program is useful in maintaining healthy relations with the public.

The educational program begins with a friendly and efficient plan for processing the patient. A cordial reception, a pleasant and relaxed office environment, confident and efficient office personnel, and prompt individual attention produce a receptive attitude for the instruction period held at the end of the consultation.

Instruction Room

The heart of the program is the instruction room. Ideally, the patient progresses from the reception area to the consultation and examining rooms and finally arrives at a special room which has been equipped and planned for educational purposes. In more restricted quarters, a consultation or examining room may be used, but whenever possible a separate room should be allocated for education and instruction. It is in this room that the patient listens to a summary of his examination and receives recommendations for treatment. His condition is explained in language tailored to the individual's intellectual capacity and experience. The treatment program is then described in great detail. The instruction room is equipped with comfortable chairs for the patient and responsible relatives. A screen and slide projector, chalk board, anatomic models, home treatment apparatus, and printed instruction material are displayed for use by the instructor.

Part of the instruction must be made by the physician. However, many of the details may be related by an office assistant. In this way the time of the physician may be effectively conserved without loss of any of the physician's authority or effectiveness as manager of the problem. Equipment and materials for instruction cannot be provided for every conceivable condition or circumstance. However, in private practice, certain problems are encountered frequently and it is practical to prepare educational aids to illustrate such common medical problems.

Persons who are suffering from disabling, painful, or serious conditions usually require less instruction than patients with less urgent problems. Seriously afflicted individuals are usually admitted to a hospital where they may be indoctrinated regarding their problem in the course of bedside visits. The instruction room serves those persons who will be seen infrequently by the physician and who will be expected to carry out a program of treatment at home. It is this latter group that makes up the majority of office patients, and this fact makes the instruction room feasible and useful.

Printed Instructions

A patient cannot be expected to grasp and remember more than the general facts related to his medical problem and treatment program from verbal and visual instruction, therefore it is important to present the patient with detailed printed instructions. These instructions cover such items as (1) information about a specific condition, (2) out-

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line of the treatment program, (3) directions concerning a drug, and (4) diagrams of equipment to be constructed or used at home.

If the patient receives printed instructions, the recommended therapy may be carried out more accurately and effectively. The patient becomes convinced that the doctor is taking his problem seriously, and his approval of this systematic approach ensures improved therapeutic results. An example of instructions for patients with low-back conditions reads as follows: What to do: arrange for extra rest each day; sleep on firm bed; sit in straight-back chair; keep warm when exposed to cold; apply warmth to lower back; use firm backrest in automobile; plan some personal activities each day; bend and lift with knees and hips; take frequent doses of aspirin for pain; visit your physician at regular intervals. What to avoid: bending and lifting with back; moving or pushing heavy objects; lifting awkward or heavy objects; sports involving twisting movements; excessive heat applications; dependence on appliances; driving in heavy traffic or on rough roads; unnecessary exposure to cold; unusual physical exertion; prolonged inactivity; anxiety and discouragement.

This printed material may be prepared with use of standard duplicating equipment. With a few hours of work the physician and his secretary will be able to prepare instruction material that will last for months and save countless hours of the physician's time.

Anatomic Models

Scientific firms offer a variety of anatomic models that may be purchased for office use. No amount of talk can equal the effectiveness of a model of a protruded disk shown to a patient suffering from such a condition. Most of the suffering from an illness is caused by anxiety arising from what is taking place. Models that demonstrate the problem will dispel much anxiety in a wide variety of medical problems.

Visual Instruction

Many treatment programs are suitable for visual instruction. About two dozen slides on the care of painful neck and arm problems may effectively show the patient how to manage his problems successfully at home. A semiautomatic slide projector is ideal for this purpose. Sets of slides may be stored in cassettes and projected as the need arises. This plan reinforces what has been said to the patient and enables him to understand instructions supplied on printed form. This part of the program is especially applicable for delegation to an office assistant. If the visual instruction system illustrates most common conditions, the physician will soon notice a reduction in fatigue after a day in the office.

Chalk Talks

Conditions encountered occasionally may be explained by chalk diagrams. This experience of making on-the-spot illustrations for patients is excellent training for making similar chalk talks when testifying in jury trials and during lectures to other physicians.

The Instructor

Instruction is shared by the physician and his office assistants. Registered nurses make the best instructors because of their background and experience. After listening to the doctor instructing several patients, the nurse can usually take over the instruction program. Assistants employed in this capacity should be encouraged to take an interest in this special teaching and to contribute their own ideas and methods to the project.

The Office Health Exhibit

The physician's office is a public place. This setting provides an opportunity to indoctrinate the public on general health subjects. A large bulletin board may be used for a health exhibit. It is practical to prepare and change the subject matter quarterly. Accident prevention in the home, swimming safety rules, proper use of firearms, and good driving practices are some of the subjects that may be illustrated.

Hospital Instruction

Certain parts of the instruction system are useful for the education of hospital patients. A supply of forms may be stored at the hospital for presentation to patients. A portable viewer and collection of slides may be employed by an office assistant to instruct patients in measures to be carried out at home. Some of the small anatomic models may also be employed in the hospital program.

Surgical Specimens and Roentgenograms

An integral part of the hospital education program is the viewing of roentgenograms and surgical specimens by the patient or relatives. Most pathological conditions seen by the physician on roentgenograms may be pointed out to the patient and responsible relatives. Patients are better satisfied when they have seen their problem on an x-ray film, and in some respects they are entitled to this consideration since they pay for this special examination.

In most surgical specialties it is advisable to request that a relative be present at the hospital during an operation. At the conclusion of the surgical procedure, the surgeon may report directly to the family regarding the condition of the patient. This conference provides an excellent opportunity to show the surgical specimen. The material should be dressed up for viewing by washing away the blood and neatly arranging the specimen on a clean white surface. Viewing the parts that have been removed dispels much of the mystery and disbelief that might otherwise result in the months that follow. This procedure is especially important in malignancy problems.

Postoperative Instruction

The patient who has experienced a major surgical operation presents a special psychological management problem when he leaves the security of the hospital. Previously, he has received some instruction about his condition and what has been done surgically. As soon as he arrives home, a host of anxieties confront him. His progress at home can be facilitated and smoothed by special printed postoperative instructions.

Community Education

The physician may make his work easier in the community if he takes advantage ot opportunities to discuss his work with interns, residents, nurses, and laymen. This policy is especially important in the surgical specialties. A little extra effort to enlist the interest and understanding of associates and the public will result in improved work efficiency.

Summary

A program for the education and instruction of patients is a useful method of improving treatment results and maintaining good public relations. The instruction room is the heart of the program. Visual aids, printed instruction forms, and demonstrations are used by the physician and his assistant to indoctrinate the patient regarding his condition and what may be done to alleviate it. Other methods include the office health exhibit, instruction in the hospital, and lecturing to medical lay groups. The modern patient appreciates a physician who takes the trouble to describe his condition in ways he can understand and then outlines a specific program of treatment.

316 W. Broad St.

CLINICAL NOTES

LYMPHADENOPATHY INDUCED BY ETHOTOIN (PEGANONE)

CLINICAL AND PATHOLOGICAL MIMICKING OF MALIGNANT LYMPHOMA

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and
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Ethotoin (Peganone), an anticonvulsant drug with the formula 3-ethyl-5-phenylhydantoin, first introduced in 1956,[1] may produce clinical and pathological alterations similar to malignant lymphomas. If this condition is not recognized as a drug reaction rather than a neoplasm, such therapy as nitrogen mustard or irradiation may be instituted and the patient or his family may be told that he has an incurable disease. The following case forcibly brought this to our attention.

Report of a Case

A 7-year-old mentally retarded boy was admitted to St. Louis Children's Hospital Nov. 21, 1957, with a seven-week history of cervical lymphadenopathy. A diagnosis of "convulsive disorder" was made when the child was 3 years of age. The patient had a history of a marked allergic rhinitis. Recent therapy included metharbital (Gemonil) and mephobarbital (Mebaral). In September, 1957, 0.25 Gm. of ethotoin given twice daily was added to the regimen and increased to 0.5 Gm. given twice daily about six weeks prior to admission.

Seven weeks before admission, the patient developed a cold, which was accompanied by the development of slightly enlarged, tender inguinal lymph nodes. These subsequently returned to normal. Six weeks prior to admission, he developed on the right side a cervical lymphadenopathy which was stated to be "as large as a fist." After this, cervical adenopathy on the left side and small axillary nodes were noted. There was no history of weight loss or rash.

On physical examination at the time of admission, prominent, slightly tender cervical nodes were present bilaterally. These ranged in size from 1 by 1 by 2 cm. to 2 by 4 by 6 cm. The liver and spleen were each felt 1 cm. below the respective costal margins. No rash was present. The white blood cell count on admission was 10,650 per cubic millimeter, with a differential count that included 4% eosinophils, 31% neutrophils, 44% lymphocytes, 9% monocytes, and 2% basophils. On another differential count, there were 15% eosinophils. The hemoglobin level was 13.2 Gm. per 100 cc. Both old tuberculin and histoplasmin skin tests were negative, as was a heterophil antibody titer. A bone marrow examination was normal, except for a slight increase in eosinophils. The temperature ranged from 37.4 C to 39.2 C (99.3 to 102.2 F), although at no time did the child appear acutely ill.

Clinically, the diagnosis was malignant lymphoma, probably Hodgkin's disease, because of the adenopathy, hepatosplenomegaly, and normal bone marrow. A biopsy specimen was taken from a cervical lymph node on the right side on Nov. 22, 1957.

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On gross examination, the node was pale yellow-gray on the external surface; when sectioned, it had a nodular appearance and was pale gray to ivory, with some hemorrhagic areas. It measured 1.5 by 1 by 1 cm. Microscopically, the normal nodal architecture was almost completely replaced by a very pleomorphic cellular pattern, which included lymphocytes, plasma cells, neutrophils, eosinophils, and large reticulum cells (see figure). No definite Sternberg-Reed cells were seen. A few normal sinuses were noted. Most spectacular was the marked necrosis in areas of the node, accompanied by phagocytosis of nuclear debris. Many of the reticulum cells and lymphocytes were larger than normal and varied considerably in size and shape. The nuclei were slightly pleomorphic, with prominent nucleoli and frequent mitotic figures. A few lymphocytes invaded the capsule. This combination of loss of architecture, pleomorphism of cells, prominent nucleoli, mitoses, and invasion of the capsule strongly suggested a diagnosis of malignant lymphoma.

Because of our experience with other anticonvulsants, the possibility that this adenopathy also might be related to a hydantoin drug was considered by the pediatricians and the pathologists. Therefore, after the biopsy was performed, the ethotoin was withdrawn. Within a matter of days, the fever subsided and the lymph node enlargement had all but vanished. At the time of writing, four months later, there is no lymphadenopathy. The esoinophilia and hepatosplenomegaly have also disappeared. The child appears in perfect physical health, with no abnormal clinical or laboratory findings. He is receiving no medication for his seizures, which now occur no more frequently than when he was receiving the several drugs.

Comment

This case, both clinically and pathologically, is an example of the lymphadenopathic reaction to hydantoin and hydantoin-like drugs similar to those that have been reported before and that we are reviewing in another paper.[2] Six other patients with similar cases have been admitted to St. Louis Children's Hospital or to Barnes Hospital. Clinically, this reaction usually starts one week to a few months after institution of the specific drug therapy. Fever, exanthema, and eosinophilia, in various combinations, accompany the adenopathy. The node enlargement varies considerably in degree. After cessation of therapy with the offending drug, the nodes return to normal size in about one month or less and the other symptoms and signs disappear quickly.

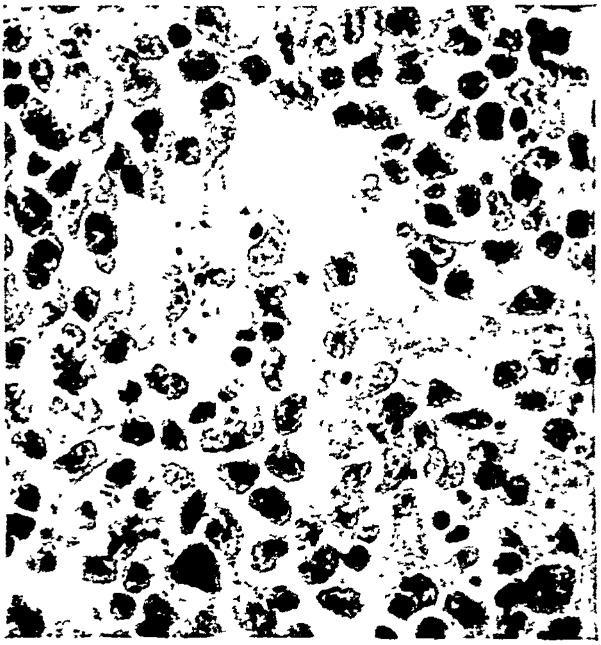
Pathologically, this case is also quite typical of others we have seen in that it shows obliteration of the normal nodal architecture, infiltration with reticulum cells, plasma cells, and, especially, eosinophils, frequent mitoses, foci of necrosis, and phagocytosis of nuclear debris.

The importance of recognizing this entity, as stated above, is distinguishing it from the various malignant lymphomas. By combining the clinical history with the pathological findings, this usually can be done. Certainly, the anticonvulsant drug should be withdrawn and the patient's course observed before any therapy directed at a malignant lymphoma is instituted.

The reactions to ethotoin reported previously[3] include skin rash which disappeared on cessation of therapy, gastrointestinal symptoms, dizziness, nystagmus, diplopia, drowsiness, headache, tension, and depression. Gingival hyperplasia and ataxia have occurred only in patients also receiving other hydantoin drugs. No blood dyscrasia or hepatic or renal dysfunction has been reported. However, monthly blood cell counts and urinalyses, and hepatic function tests when indicated, are recommended.[4]

Summary

Therapy with ethotoin (Peganone), as with other hydantoin and hydantoin-like drugs, can lead to striking enlargement of lymph nodes, hepatosplenomegaly, fever, and eosinophilia. These clinical findings, plus the changes seen in biopsies of lymph nodes, can lead to an erroneous diagnosis of malignant lymphoma. Stopping treatment with the drug results in remission of the adenopathy, fever, and eosinophilia. This condition, which is felt to be allergic in origin, must be distinguished from the various malignant lymphomas.



Section of cervical lymph node showing pleomorphic reticulum cells, eosinophils, lymphocytes, necrosis, and phagocytosis (hematoxylin and eosin, × 750).

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TRANSILLUMINATION OF PARANASAL SINUSES

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I have often been impressed by the importance placed by medical students and some physicians on transillumination of the paranasal sinuses. The presence or absence of clear transillumination is sometimes regarded as a significant sign, without consideration of other physical findings or the type of skull being transilluminated. Otolaryngologists, in general, regard transillumination as a confirmatory sign of limited value and evaluate it on the basis of the history and the information obtained on anterior and posterior rhinoscopy. A record of a previous examination is advantageous for comparison. The test is regarded as negative if the sinuses transilluminate equally and well; if one or both sinuses show impaired transmissibility of light, the test is regarded as positive.

Fundamentally, the findings on transillumination are uncertain because of the many variable factors: the intensity of the illumination, the darkness of the room, pigmentation of the skin, and the thickness of the facial bony structure. For anatomic reasons the value of transillumination in diagnosing frontal sinusitis is more limited than in maxillary sinusitis. A small or absent frontal sinus or a thick anterior wall is sometimes interpreted as an opaque sinus. The antrums are more uniform in size and offer a better opportunity for examination, especially in contrasting the two sides. If both sides are affected, the value of transillumination is diminished. In men with a heavy superior maxilla the sinuses may transilluminate poorly or not at all, whereas on x-ray examination the sinuses may appear quite normal. On the other hand, children, or women with a slight bony structure, may exhibit sinuses that transilluminate clearly but evidence an opaque antrum on x-ray study. For this reason transillumination in children is known to be unreliable. Less well known is the fact that transillumination is of debatable value in most women, except in the presence of a unilateral opacity of considerable degree, when the comparison of the two sides indicates a definite difference.

To demonstrate this opinion I compared my findings on transillumination with the results of the x-ray examination in 100 patients. The transilluminator was placed behind the lower rim of the orbit and the palatine light reflex was noted through the open mouth, with the intensity of the illumination varied by means of the rheostat on the battery handle. All of the patients had symptoms referable to the sinuses, and this study was a part of a routine otolaryngological office examination. An attempt was made to classify the degree of maxillary sinus opacity on the basis of 0 to 4+, 0 representing a clear sinus and 4+ a dense opacity. If the difference between the two types of examination was found to be 2+ or more on one or both sides, the result was recorded as no correlation. No mention will be made here of the cause of the opacity, whether it be a thickening of the sinus mucous membrane, inflammatory or allergic edema, empyema, cyst or tumor, or the finer changes in the bony structure and sinal mucosa visible on radiologic examination. The presence of an opacity of any kind, even if transitory, is regarded as an abnormal reading.

In the adult males of this series, 3 out of 23 patients did not have findings that correlated; therefore in 13% of the men the results on transillumination and the x-ray reading failed to correspond. The women in this series showed 22 out of 55 cases not correlated; therefore 40% of the findings in women did not correspond. Finally, in children 14 out of 22 cases did not correlate; therefore in children 63% of the findings did not correspond.

Comment

Historically, electric transillumination or diaphanoscopy was introduced by the Polish laryngologist, Heryng, in 1889.[1] The older clinicians stressed the

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importance of the examination especially when done under rheostat control, judging the loss of translucency by changing the intensity of the illumination. The transoral method was used, assessing the light reflex on the cheek, the lower orbital ridge, and in the pupil. An experienced observer was said to be able to distinguish between dulness caused by pus in the antrum and complete darkness caused by a tumor. However, the limitations of the test were well recognized. It was known that an absence of the infraorbital light reflex was possible when the bone was very thick or a small sinus cavity was present, and negative diaphanoscopic result did not necessarily mean the sinus was not affected.[2]

There is little doubt that a larger series of comparisons would yield a less dramatic difference between sexes and between adults and children than in this group of patients. However, these figures substantiate an estimation long held of the limited value of transillumination. The correlation in men was better than anticipated. The figures definitely indicate that in women and especially in children transillumination can not be relied upon as a diagnostic test. A surprising number of women and children in this series presented a masked sinusitis, in which the entire clinical examination was negative and the diagnosis was made on the basis of the x-ray examination and antral irrigation.

Conclusions

Transillumination of the paranasal sinuses should be regarded as a confirmatory or supplementary test. In men some reliance can be paid to a positive or negative test. In women and children only a positive test can be regarded as significant.

139 S. Main St.

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EVALUATION OF A NITROPRUSSIDE DIP TEST FOR KETONE BODIES

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and
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The detection of ketone bodies in urine specimens is sufficiently important to warrant the inclusion of a nitroprusside test for ketonuria as a part of the routine urinalysis. In the past, methods available have included a tablet test (Acetest) and the Rothera test, a conventional test tube procedure. Recently the nitroprusside test for urine ketones has been made available as a stick or dip test with a preparation called Ketostix. This test, like the other nitroprusside tests, depends on the reaction between acetoacetic acid and nitroprusside to produce a colored complex. In order to determine the accuracy and simplicity of the new test, it was compared with the two more standard procedures on a series of routine urine specimens in a general hospital laboratory. Tests were also carried out by experienced and inexperienced personnel on urines with and without added acetoacetic acid. The present report describes the results obtained in this study.

Methods

Acetest.—Acetest is a tablet consisting of sodium nitroprusside, sodium phosphate, and glycine. The tablet is placed on a clean surface, such as a piece of typing paper. It is moistened with a drop of urine, and 30 seconds later the color of the tablet is compared with a color chart with three colors ranging from lavender to purple and representing trace, moderate, and strongly positive reactions. Reactions were graded as trace, moderate, strongly positive, or very strongly positive.

Ketostix.—Ketostix consists of a stiff cellulose strip impregnated with sodium nitroprusside, glycine, and buffered sodium phosphate. A strip is dipped in a urine specimen and placed on a clean surface, such as a piece of typing paper. Exactly one minute later, the color of the stick is compared with three color blocks on the label of the bottle of Ketostix. Colors ranging from pink to purple represent small, moderate, or large amounts of ketone bodies. Positive reactions were graded as trace, small, moderate, or large.

Attending Physician, Grant Hospital of Chicago, and Clinical Instructor, Department of Medicine, University of Illinois College of Medicine (Dr. Chertack), and Pathologist, Grant Hospital of Chicago, and Clinical Assistant Professor of Pathology, University of Illinois College of Medicine (Dr. Sherrick).

Rothera Test.—Approximately 0.5 Gm. of solid ammonium sulfate is placed in a small test tube. Approximately 3 ml. of urine and 3 drops of freshly prepared 5% sodium nitroprusside are added and mixed well. One to 2 ml. of concentrated ammonium hydroxide is stratified on the mixture, and two minutes later the interface of the solutions is observed for a purple color. Reactions were graded negative, trace, 1+, 2+, 3+, or 4+, according to the intensity of color.

Plan of Experiments.—The regular technician examined by means of Acetest each urine specimen as received in the laboratory. Without any knowledge of the results obtained, a second technician then carried out reactions with Ketostix, Acetest, and the Rothera test. Reactions by each method were recorded separately. After this, the first technician's results were obtained, and all four results were recorded on a master tabulation sheet. Any specimens which gave a positive reaction with all four nitroprusside tests were tested additionally for acetoacetic acid with Gerhardt's ferric chloride test and with Lindemann's test. Twofold serial dilutions (made with a negative specimen) were made of most specimens which gave a moderate or stronger reaction with the nitroprusside tests. These dilutions were tested with Acetest and Ketostix.

TABLE 1.—*Results with Acetest and Ketostix on Twofold Serial Dilutions of Positive Urines*

	Urine Dilution*													
Specimen, No.	Undiluted		1:2		1:4		1:8		1:16		1:32		1:64	
	A	K	A	K	A	K	A	K	A	K	A	K	A	K
1	2+	2+	1+	1+	1+	Tr	0	0	...	...	...	...	...	...
2	4+	4+	3+	2+	2+	2+	1+	1+	Tr	1+	Tr	Tr	0	0
3	4+	4+	4+	3+	3+	2+	2+	2+	1+	1+	Tr	Tr	0	0
4	2+	1+	1+	Tr	Tr	Tr	0	0	...	...	...	...	...	...
5	2+	1+	1+	1+	Tr	Tr	0	Tr	0	0	...	...	...	...
6	4+	3+	2+	3+	2+	2+	1+	1+	Tr	Tr	0	0	...	...
7	2+	2+	1+	1+	1+	Tr	Tr	Tr	0	0	...	...	...	...
8	3+	2+	2+	2+	1+	1+	Tr	Tr	0	0	...	...	...	...
9	3+	3+	2+	2+	2+	2+	1+	1+	Tr	Tr	0	Tr	0	0

* A indicates Acetest and K, Ketostix. Reading of 4+, darker than darkest color on charts; 3+, darkest color on charts; 2+, middle color on charts; 1+, lightest color on charts; and Tr, lighter than lightest color on charts

In addition, 10 mg.% and 100 mg.% of acetoacetic acid were added to aliquots of every urine specimen. These samples were all then tested with Acetest and Ketostix.

Results

Of the 185 urine specimens studied, perfect agreement was obtained on 178 samples. Of the specimens, 158 gave negative results with all four tests (Ketostix, Rothera, and Acetest by each of two technicians), 8 specimens gave trace or 1+ results with all four tests, and 12 specimens gave positive reactions stronger than trace with all four tests. Trace-negative results were obtained on 7 specimens. Five out of the seven specimens gave trace reactions with the Rothera test and negative reactions with the other nitroprusside tests. This is logical since this modification of the Rothera procedure is very sensitive.[1] The other two specimens also showed minor differences and probably contained a minimal amount of ketone bodies quite likely below the pathological range. (One showed trace reaction to all but first Acetest; one, trace to second Acetest and Rothera test and negative reaction to other tests.)

All urine specimens containing 10 mg.% of added acetoacetic acid gave a small or trace reaction with both the stick test and the tablet test. All urine specimens containing 100 mg.% of added acetoacetic acid gave a large or strongly positive reaction with both tests. This indicated that nothing excreted in the urine of a variety of hospital patients receiving a variety of drugs and medicaments interfered with the detection of ketones by either the stick or the tablet nitroprusside test.

Results with Acetest and Ketostix on twofold serial dilutions of all urine specimens which gave stronger than a trace-positive reaction are shown in table 1. It is obvious that the stick test and the tablet test have approximately the same sensitivity. Each positive specimen was carried through a diffusion procedure with use of Conway micro diffusion units to estimate the amount of nitroprusside color which was due to acetone and the amount due to acetoacetic acid.[2] All 12 urine specimens showed that 96% to 99% of the color obtained in the nitroprusside reaction (with Acetest) was due to acetoacetic acid and that only 1% to 4% of the color was due to acetone.

Each of the 12 urine specimens was also diluted 1:10, 1:20, and 1:50 with a negative specimen. Reactions of each of these dilutions with Acetest were compared with reactions obtained with standard solutions of 2, 5, and 10 mg. of acetoacetic acid added to 100 ml. of urine. In this way a rough estimate of the acetoacetic acid concentration was made. Table 2 shows the estimated acetoacetic acid concentration of each of these specimens and the results obtained with Gerhardt's ferric chloride test[1] and with Lindemann's test.[3] Those urines which gave only trace reactions were not diluted but are listed in the table as containing not more than 20 mg. of acetoacetic acid per 100 ml., since Acetest always gives more than a trace reaction with acetoacetic acid concentrations over 20 mg.%. It is obvious from this table that neither of the so-called acetoacetic acid tests has a very great sensitivity. Only three clear-cut positive reactions were obtained with the ferric chloride test, and these were on urine specimens containing 100 to 150 mg. of acetoacetic acid per 100 ml. Only one positive reaction (on a specimen containing 150 mg. of acetoacetic acid per 100 ml.) was obtained with Lindemann's test. This urine specimen gave a very strongly positive reaction with the nitroprusside tests. It is also obvious that the ferric chloride test is nonspecific, since six drug reactions (color stable to boiling) were obtained which either masked the acetoacetic acid reactions or were given by urine specimens containing less than 20 mg. of acetoacetic acid per 100 ml.—a concentration far below the limit of sensitivity of this test.

All nitroprusside tests react with both acetone and acetoacetic acid, but all are much more sensitive to acetoacetic acid than to acetone. With Ketostix, this difference in sensitivity is even greater than with other nitroprusside tests, so that for all practical clinical purposes Ketostix is specific for acetoacetic acid. It has been shown that most of the nitroprusside color in positive reactions on ketotic urine specimens arises from acetoacetic acid rather than acetone.[2] Therefore, Ketostix, because of its specificity and high sensitivity, possesses a distinct advantage over the nonspecific, insensitive ferric chloride tests and over the insensitive Lindemann's test for acetoacetic acid.

Reactions with Ketostix Obtained by Persons Unfamiliar with the Test.—In order to define the simplicity and accuracy of Ketostix in detection of urine ketones, acetoacetic acid was added to several negative urine specimens in amounts of 5, 10, 25, 50, 100, or 200 mg. per 100 ml. These specimens were then coded and tested as unknown specimens with Ketostix by various members of the Grant Hospital laboratory staff, including clerical personnel as well as technically trained personnel. None of these people had ever used Ketostix before, and their results in detecting ketones in "unknown" urine specimens were surprisingly good. A total of 260 tests were carried out by inexperienced persons, and the results are tabulated in table 3 along with results obtained in 50 tests by a technician experienced in the use of Ketostix. Since exactly the same number of tests was not carried out at each level of acetoacetic acid concentration, results have been expressed as the percentage of tests at each given concentration which gave each designated reaction. Excellent agreement is shown between results obtained by experienced and inexperienced people. With trace amounts of acetoacetic acid (5 or 10 mg.%) it is to be expected that an experienced technician would obtain more consistently positive results. Table 3 shows this to be true in this experiment. However, over 90% of the tests at the 10-mg. level and 60% of the tests at the 5-mg. level were called positive by persons who had never used the test before.

TABLE 2.—*Reactions of Nitroprusside-Positive Urines with Acetoacetic Acid Tests*

Specimen, No.	Estimated Acetoacetic Acid Concentration, Mg. %	Reactions with Acetoacetic Acid Tests: Gerhardt's Ferric Chloride	Reactions with Acetoacetic Acid Tests: Lindemann's Test
1	under 20	0	0
2	40	+(drug)	0
3	under 20	+(drug)	0
4	100	+	0
5	150	+	+
6	50	0	0
7	40	+(drug)	0
8	under 20	0	0
9	100	+	0
10	under 20	0	0
11	under 20	0	0
12	under 20	+(drug)	0
13	under 20	0	0
14	under 20	+(drug)	0
15	50	0	0
16	50	0	0
17	80	slight +	0
18	40	+(drug)	0

TABLE 3.—*Results with Ketostix by Experienced and Inexperienced Personnel on Urine Specimens With and Without Added Acetoacetic Acid in Three Hundred Ten Tests*[*]

Acetoacetic Acid Added, Mg. %	Tests by Inexperienced Personnel					Tests by Experienced Personnel				
	Large	Moderate	Small	Trace	Negative	Large	Moderate	Small	Trace	Negative
200	100	...	...	...	...	100	...	...	...	...
100	89	11	...	...	...	100	...	...	...	...
50	15	85	...	...	...	29	71	...	...	...
25	...	46	54	...	...	...	57	43	...	...
10	...	...	71	20	9	...	...	71	29	...
5	...	...	20	40	40	...	...	...	80	20
0	...	...	...	...	100	...	...	...	...	100

[*] Numbers are the percentage of tests at each level of acetoacetic acid which gave the designated reaction.

Use of Ketostix and Acetest in Detection of Serum Ketones.—A total of 96 serum samples were tested with Ketostix and Acetest for detection of serum ketones. Results on all samples were negative with both tests. To 40 of the samples dilute aqueous acetoacetic stock solution was added to give 10-25 mg.% of acetoacetic acid in serum. These samples were then tested again with Ketostix and Acetest, and all results were trace, small, or moderate, with the moderate reactions being obtained on these samples containing 25 mg.% of acetoacetic acid. The technique for use of Ketostix on serum is the same as that for urine. However, since the high protein concentration of serum prevents the absorption of the drop of serum by the tablet of Acetest, it is necessary to add two drops of water to the drop of serum on the tablet. This makes the developing color easier to see and does not significantly affect the sensitivity of the test. It is considered that this application may be of importance in the management of diabetic acidosis and further investigation is being carried out.

Summary

Ketostix, a new nitroprusside stick test for urine ketone detection, has been compared with a tablet nitroprusside test (Acetest) and the test tube Rothera procedure on a series of urine specimens in a large city hospital. Results indicate that good agreement is obtained with Ketostix and Acetest but that the Rothera modification used is some-

what more sensitive. A series of 260 tests with Ketostix on negative urine specimens with and without added acetoacetic acid was carried out as "unknowns" by laboratory personnel who had had no previous experience with the test. Results obtained were those to be expected from the amounts of acetoacetic acid added and agreed well with results obtained on the same specimens by experienced personnel. Ketostix appears to be a satisfactory, simple but accurate test for routine detection of ketones in urine and serum.

840 S. Wood (Dr. Chertack).

The nitroprusside stick and the nitroprusside tablet used in this study were supplied as Ketostix and Acetest by the Ames Company, Inc., Elkhart, Ind.

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TRANSISTOR FOR TRANSMISSION OF ELECTROCARDIOGRAMS BY TELEPHONE

A UNIT WHICH DOES NOT REQUIRE ELECTRICAL CONNECTION TO TELEPHONE

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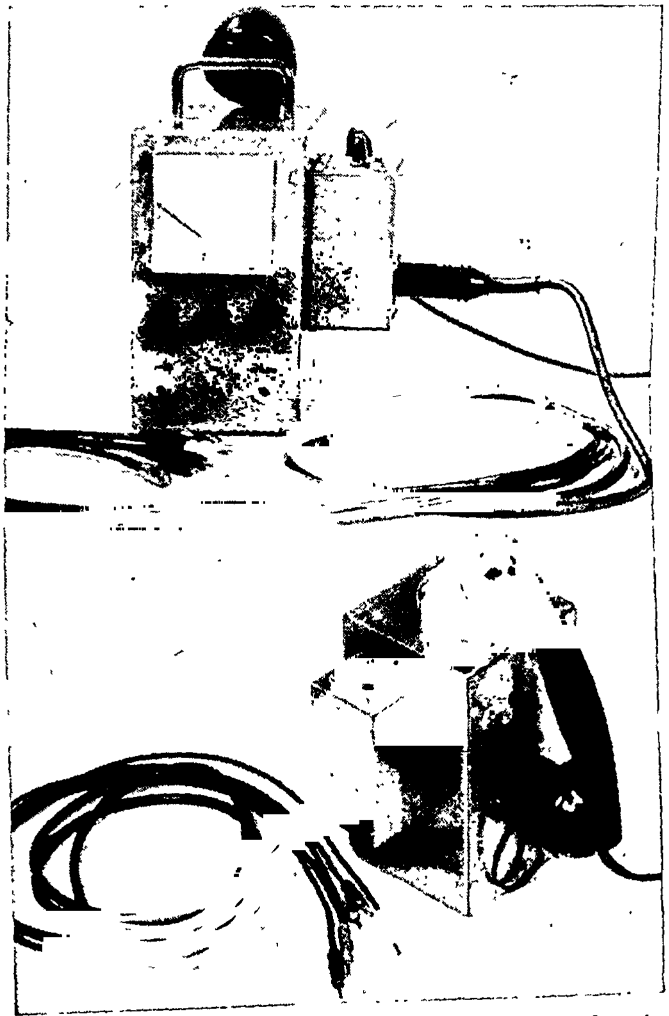
The possible value of a method of transmitting the electrocardiogram and heart sounds over standard telephone lines has intrigued workers since the time of Einthoven.[1] Practical usefulness of the idea has been limited, first, by the bulkiness of the equipment, second, by the necessity for some means of electrical connection between the patient, the electrocardiograph machine, and the telephone, and, third, by the need for special permission from the telephone company for connection and transmission.

At this laboratory, a small, 5-lb., transistorized unit has been developed which can be attached directly to the patient by standard lead wires and which needs to be placed only adjacent to the mouthpiece of any standard telephone. The signal is transmitted into the mouthpiece of the telephone by inductance, and no wire connection is necessary. Routine or local long-distance lines carry the signal without special arrangement with the telephone company. The transmission of the electrocardiogram can be interrupted at any time and additional information offered by the operator. A multiple-lead selector is built into the unit. The unit does not need an electrical outlet; it is powered by pen-light and mercury batteries.

In addition, with a standard heart-sound microphone, heart tones and murmurs can be transmitted over standard telephone lines with excellent quality. At the receiving end, a similar unit, slightly



Front view (*above*) and side view (*below*) of entire transmitting unit plus telephone.

From the Cardiovascular Laboratory, University of Kansas Medical Center.

modified, can take the information from the telephone and signal any standard electrocardiograph machine.

Description

The transmitter is essentially a highly sensitive frequency modulator, with a rather unique, three-stage, push-pull type of a transistorized, sensitive, 60-db. direct-current amplifier which is linear from approximately 1 cps to well above the requirements for this use. The frequency-modulated tone output of 1,300 cps is accomplished with use of two Hartley oscillators, one oscillating at 65 kc. and the other at 66.3 kc., beating together to produce the 1,300 cps frequency which then is modulated plus and minus about 400 cps. Inasmuch as the 65-kc. oscillator may be modulated up by introducing a plus potential and the 66.3-kc. frequency modulated down by introducing a plus potential into the amplifier, great frequency change may be accomplished with a very small potential change in the output. A two-position switch permits the Hartley oscillators to be either in or out of the circuit. When the switch is in position to eliminate the Hartley oscillators, the instrument can be used as an amplifying stethoscope. The instrument is powered entirely by batteries. A pen-light cell operates the first stages of the direct-current amplifier which draw approximately 40 μa and thus are never turned off, because their life will be about shelf life with this amount of current being drawn from them. The final stage of the amplifier uses 13 V of mercury battery, and the remainder of the equipment uses 6.5 V of mercury battery.

Uses

This apparatus seems to solve most of the problems which have interfered with the possible civilian and military use of such an instrument. Consultation at any distance with use of standard telephone lines without special permission or electrical connection is possible. Electrocardiograms and heart sounds can be transmitted; the transmission can be freely interrupted for comment or question. The instrument is very small, yet rugged.

Electronic engineering was done by Mr. John Walker.

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DIAGNOSTIC PROBLEMS

FULMINANT POLYARTHRITIS, FEVER, AND CUTANEOUS NODULES IN AN ALCOHOLIC PATIENT

Clinical Pathological Conference (PM 1068-57), Oct. 31, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul B. Szanto, M.D.

Clinical Data

A 57-year-old garage mechanic entered Cook County Hospital on July 23, 1957, because of joint pains. He had been in good health until 14 days prior to admission when, following trauma, his left ankle became swollen, red, and painful. Four days later the other ankle was similarly affected. He subsequently noted temperature elevation to 102 F (38.8 C), chills, and painful swelling of both elbows and both knees. He failed to respond to penicillin therapy and was referred to the hospital.

Systemic review disclosed nocturia (six times a night) and diarrhea. His history included appendectomy in 1925, carbon monoxide poisoning in 1952, some joint pains during the winters, especially with changes in the weather, but no sore throats. His fiancee stated that on three or four occasions in the previous two years he had had severe abdominal pain lasting several hours. He habitually consumed two quarts of beer and eight shots of whisky daily. His father and one brother had died of coronary disease.

Physical examination revealed an acutely ill, confused, well-developed, and well-nourished white man with a rectal temperature of 104 F (40 C), pulse 124, respirations 32 per minute, and blood pressure 120/70 mm. Hg. On the left calf there were three red papular lesions about 5 to 10 mm.

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Dr. Zimmerman is Chairman, Department of Medicine, Mount Sinai Hospital, and Professor and Chairman, Department of Medicine, Chicago Medical School.

in diameter. The ankles, knees, elbows, and wrists were hot, red, swollen, fluctuant, and very tender. There was also a painful swelling of the right second and fifth metacarpophalangeal joints and some tenderness on passive movement in both shoulders and both hips.

Urinalysis revealed a specific gravity of 1.015, acid reaction, 2+ albumin, and no sugar, acetone, or urobilinogen. The sediment contained 3 to 4 leukocytes per high-power field, bacteria, and rare granular and hyaline casts. The hemoglobin level was 60%, erythrocytes 3,710,000 and leukocytes 19,000 per cubic millimeter, with 40% polymorphonuclear leukocytes, 53% stab cells, 4% lymphocytes, 3% monocytes, normal platelets, 3+ toxicity, Döhle bodies, and rouleaux. The sedimentation rate was 60 mm. per hour and hematocrit reading 26%. L. E. cell preparations were negative. Blood Wassermann and Kahn reactions were negative. Blood culture was negative. A joint aspirate culture grew nonhemolytic Staphylococcus pyogenes var. albus on one occasion and was subsequently sterile. Stool cultures revealed no pathogens. Agglutination tests for Salmonella and Brucella were negative. A tuberculin skin test was negative (1:10,000). An electrocardiogram showed only sinus tachycardia. Total protein in the joint fluid was 3.4 Gm. per 100 ml. On Aug. 3 and 4, the serum amylase level was 512 units. On Aug. 7, it was 256 units. (See table 1 for additional biochemical data.)

Table 1.—*Biochemical Data Obtained from Laboratory Studies on Patient*

Constituents	Dates and Laboratory Values						
	7/25	8/1	8/3	8/5	8/6	8/7	8/8
NPN, mg./100 ml.	26	34	...	...	32	32	30
Uric acid, mg./100 ml.	4.5	7.0	...	...	5.8	5.2	4.9
Albumin, Gm./100 ml.	2.3	...	...	...	2.1	2.4	...
Globulin, Gm./100 ml.	3.2	...	...	...	1.9	1.8	...
Phosphorus, mg./100 ml.	...	4.3	...	4.6	4.0	2.9	...
Alkaline phosphatase, Bodansky units	...	...	...	...	...	3.5	...
Cephalin flocculation	2+	2+	...	...	3+	3+	...
Thymol turbidity, units	1.4	2.0	...	...	1.0	1.8	...
Gamma globulin, Gm./100 ml.	1.21	1.1	...	...	1.32	1.05	...
Cholesterol, mg./100 ml.	72	...	...	...	...	...	...
Esters, %	39	...	...	...	...	...	...
Sodium, mEq./liter	...	128	133	133	128	139	...
Chloride, mEq./liter	...	98	107	102	98	109	...
Potassium, mEq./liter	...	5.3	3.9	3.6	3.7	3.5	...
Carbon dioxide combining power, vol. %	...	...	30	26	31	...	...
Calcium, mg./100 ml.	...	9.1	...	9.2	7.8	...	...

The illness progressed steadily, and death occurred 17 days after admission. The patient's joints remained red, swollen, tender, and fluctuant. Aspiration of the joint fluid on July 24 revealed large numbers of leukocytes, but the culture was sterile. On Aug. 1, aspiration of another joint revealed crystals thought by one observer to be uric acid crystals. Colchicine was given but was withdrawn after one dose owing to marked exacerbation of the diarrhea. The joints, however, caused little distress, and the major problems were posed by vomiting, diarrhea, and progressive abdominal distention. On the seventh hospital day, the patient was cold and clammy and his blood pressure was 95/50 mm. Hg. He improved after being given an intravenous infusion of saline solution with potassium. Abdominal distention persisted despite constant gastric suction. On July 31, 900 cc. of dark brown benzidine-positive fluid was aspirated from the stomach. The abdomen was always tympanitic and often tender, but there was no rebound tenderness, and hypoactive bowel sounds were always present. The stool on Aug. 6 gave a strongly positive benzidine reaction.

On the 10th hospital day, about 20 erythematous, painless nodules were noted in the skin of the chest and abdomen. These nodules increased in number, and four days later subcutaneous nodules appeared which also rapidly increased in number. No enlarged lymph nodes were palpated. On the 14th hospital day the patient was icteric, and his urine gave positive results in tests for bile and urobilinogen. Intermittently elevated temperature to 104 F (40 C) and tachycardia persisted, unaffected by therapy. Erythromycin, chloramphenicol, penicillin, sulfasuxadine, tetracycline, and sulfisoxazole were used successively in full dosage but without effect on the abdominal symptoms, the joints, or the skin nodules. When examined on the morning of Aug. 9, the patient presented a remarkable picture. He was toxic, stuporous, febrile, and emaciated. His trunk was covered with many red cutaneous nodules, and his joints were red and swollen. Palpation of the trunk revealed innumerable, irregular, nontender nodules in the subcutaneous tissues ranging to 5 mm. in diameter. His abdomen was distended, and there was a definite though ill-defined mass occupying most of the left half of the abdomen and extending some 4 cm. across the midline. He died on the 17th hospital day.

Clinical Discussion

Dr. Hyman Zimmerman: This was a dramatic syndrome, in a middle-aged alcoholic male, of an acute severe polyarthritis with high fever, painless red skin nodules, nocturia, mental symptoms, stupor, and rapidly progressive profound cachexia. Of interest historically were several episodes within two years of severe abdominal pain, and diarrhea. The urine contained protein and sediment changes such as one sees in any severe febrile illness, especially with dehydration. Rouleaux formation observed in the blood smear was not associated with hyperglobulinemia. Leukocytosis was marked, with a striking shift to the left, and Döhle bodies were observed in the blood smear. These are degenerative changes in the leukocytes, with deposition of basophilic elements, which seem to have the same significance as toxic granulations. Döhle bodies may occur in any severe febrile illness and are not necessarily limited to systemic infection. The patient was an alcoholic and was jaundiced terminally, but there was no other evidence of severe liver disease. The esters were 39%, not depressed as markedly as one might expect with so low a total cholesterol value, in intrinsic hepatic disease.

The arthritis was described as migratory, red, hot, and fluctuant. This resembles acute rheumatic fever, but 90% of patients have their first episode of rheumatic fever before the age of 15. The oldest patient in the literature was 61. The age of 57 almost precludes this possibility. Furthermore, the skin lesions were not those ordinarily seen in rheumatic fever, and the entire course occupied only 17 days, with rapid debilitation and death, without evidence of cardiac failure. These features are not consistent with rheumatic fever. Rheumatoid arthritis can begin with dramatic acute arthritis that simulates rheumatic fever. The patient's age would be more consistent with this, but the dramatic acute onset of rheumatoid arthritis is seen in younger people. Furthermore, the rapid course is strongly against rheumatoid arthritis.

In an alcoholic man of this age, with joint disease appearing after trauma, one must consider gout. Usually gout is monoarticular in its first attack, but it does not necessarily remain so. The uric acid level was 7 mg./100 ml. on one occasion, but, in spite of this, a diagnosis of gout is not tenable. Hip and shoulder involvements are unusual, as is this type of rapidly progressive migratory arthritis. Malignant gout with a rapid course and death has been reported, but in such cases death has usually been due to renal failure, and this man did not die of renal failure.

Traumatic arthritis can be excluded because of the multiplicity of joints involved. Finally, we must consider pararheumatic arthropathy. This term has been used to refer to the joint involvement seen in some of the collagen diseases. In lupus erythematosus and periarteritis nodosa, for instance, there have been various types of joint involvement, even simulating at times the acute arthritis of rheumatic fever. Perhaps the first thing to consider is the possibility of a vascular angiitis and particularly periarteritis nodosa. In lupus erythematosus such fulminant arthritis would be unusual, but in periarteritis nodosa it is somewhat more common.

The skin lesions do not suggest erythema nodosum, in that they were distributed on the trunk and on the flexor surfaces of the limbs. Neither do they suggest embolic phenomena of bacterial endocarditis. Moreover, no cardiac murmur was described. These perhaps could represent the red, infectious, embolic phenomena of a staphylococcic bacteremia, but the blood culture was negative. Such skin lesions have been seen at times in patients with drug hypersensitivity. This brings us again to periarteritis nodosa, which is characterized by bizarre cutaneous lesions ranging from papules to areas of necrosis.

The prominent attacks of abdominal pain lasting for several hours suggest cholecystitis with cholelithiasis, ureteral stones, or even intermittent intestinal obstruction. Such pain is seen in periarteritis nodosa. About 50% of these patients have prominent gastrointestinal complaints such as pain, diarrhea, nausea, and vomiting. This man had pain and diarrhea. One would like to know whether it was diarrhea or steatorrhea. Many patients describe steatorrhea as diarrhea because they have multiple stools. This is important in considering the possibility that this patient's joint disease and abdominal complaints might be related to intestinal lipodystrophy (Whipple's disease). Fever of significant degree occurs in only 20% of these patients, and such high fever with such striking joint disease would be unusual.

Another interesting feature was the demonstration of a vague abdominal mass. In view of the elevated serum amylase levels, a pancreatic pseudocyst as a result of earlier necrosis might be suspected. The mass was left-sided but not well-defined. Nevertheless, it would be difficult to explain the total course of events by pancreatitis, even in an alcoholic. Therefore, I am inclined not to relate this mass to pancreatic pseudocyst. This could have been a neoplasm. Although joint pains have been reported in patients with neoplastic disease, I am not aware of so dramatic a joint syndrome. The mass might be a retroperitoneal hematoma, perhaps perinephric, a not uncommon complication of periarteritis nodosa. Also, an abscess, cold or hot, should be considered. The rapid development would lead one to suspect a hematoma.

Dr. Irving Greenberg: Roentgenograms of the right wrist and ankle showed much soft tissue swelling about the joint space of the ankle. A change in the trabecular pattern of the bone, together with the soft tissue swelling, suggests rheumatoid arthritis or collagen disease. Roentgenograms of the abdomen revealed marked gaseous distention of the stomach and moderate distention of the large intestine but no dilatation of the small intestine. In the adult, one rarely sees pyloric obstruction lead to such gaseous distention, but rather, the stomach fills with retained secretions. Such marked gastric ectasia suggests acute pancreatitis. This may be associated also with dilatation of the second part of the duodenum and frequently with pneumonitis with effusion. The roentgenogram of the chest showed haziness in the right lower lung field suggestive of pneumonitis. Altogether, these findings are compatible with the clinical suggestion of acute pancreatitis.

Dr. Zimmerman: My initial and final impression, however, has to be of a disease in the category of periarteritis nodosa. With these conditions, pulmonary lesions of many types are seen. I have not seen a pneumonia with a homogeneous density over an extensive area in periarteritis nodosa, unless it is due to a secondary bacterial infection. In Wegener's granulomatosis, fairly extensive areas of the lung field may be involved, but the other evidences of respiratory tract involvement expected in Wegener's granulomatosis were not present here.

In this patient, the onset was dramatic and more rapid than in most patients with periarteritis nodosa, but he did have some symptoms for several years. The high fever is consistent with this diagnosis. Renal involvement in this case leaves something to be desired; 85% of patients with true periarteritis have albuminuria and renal sediment abnormalities. Most of them will not show the so-called "telescoped urine" where elements of all three stages of nephritis are seen in the same specimen, but if one looks carefully one will see at least casts or oval fat bodies, even in the absence of azotemia. The clinical progression without azotemia is disturbing, but only half of these patients die with renal failure. The cerebral manifestations are an important clue to the presence of a disseminated disease. This patient's profound debility was entirely consistent; in fact, one of the names given to periarteritis nodosa is chlorotic marasmus, because of the extremely wasted and pallid appearance. The cutaneous and subcutaneous nodules were consistent with periarteritis to the point of being classic. Pulmonary lesions may or may not be present. Leukocytosis is characteristic of this disease, in contrast to the frequent leukopenia of lupus erythematosus. The anemia of periarteritis is most often normochromic and at times hemolytic. The jaundice which occurred was not solely hemolytic, since there was bilirubinemia, and we have no evidence for a hemolytic component. Pancreatic involvement in periarteritis has been described with serum amylase elevation and pancreatic fat necrosis. Jaundice occurs occasionally in periarteritis nodosa. It is also possible that there was underlying hepatic disease, i. e., cirrhosis, with jaundice precipitated by the superimposition of severe systemic illness.

The gamma globulin level was at the upper limit of normal. In disseminated lupus erythematosus, hypergammaglobulinemia is so frequent that one should not make the diagnosis without it; in periarteritis nodosa it is less common. The combination of low albumin and low globulin levels, in the absence of a nephrotic syndrome, suggests malabsorptive diseases or lymphoma. It may be that an intestinal lesion with an absorptive defect was associated with a periarteritis nodosa.

Dr. S. Howard Armstrong Jr.: Has Dr. Zimmerman been dissuaded from the diagnosis of septic arthritis by the absence of bacteriologic findings? I wonder how many blood cultures were done.

Dr. William Metzger: Only one blood culture was taken.

Dr. Armstrong: Was the blood count so normal that no bone marrow specimen was examined?

Dr. Steven O. Schwartz: We took no marrow specimen, so we were apparently not suspicious.

Dr. Armstrong: Platelet thrombosis may be associated with fulminating polyarthritis, but the cutaneous nodules associated with any type of acute fulminating polyarthritis are usually painful and tender. I wonder whether this should suggest a diagnosis of gout with tophaceous nodules, secondary to a lymphoma or leukemia. For the rest, I would agree with Dr. Zimmerman's diagnosis.

Dr. Earl Zaus: I was disturbed about the nodules too. Dr. Zimmerman touched on the possibility of staphylococcic septicemia, but such septicemic nodules are always painful. One type of septic nodule which is not painful, occurring in a debilitated patient, is that of miliary tuberculosis.

Dr. Frederick Steigmann: I would support the diagnosis of pancreatic disease. In favor of this diagnosis are the history of alcoholism and previous attacks of abdominal pain. We have seen patients with severely damaged pancreas who showed some of the findings observed here.

Dr. John R. Tobin: I saw this patient and had the impression that when he went to the doctor with one painful swollen joint, he was given an injection of penicillin. Some 48 hours later he developed polyarthritic disease, so we considered the possibility of hypersensitivity angiitis. I have seen one other patient with fluctuant joints and bags of fluid about the joints which broke down, and I suspect that in this patient there was a generalized arteritis and panniculitis.

Dr. Paul B. Szanto: What about a bacterial form of arthritis?

Dr. Tobin: I would agree with Dr. Zimmerman's conclusions regarding the septic arthritis.

Dr. Zimmerman: With respect to the possibility of the skin lesions being tuberculous, these did not sound like tuberculids. I would not be surprised if this is a necrotizing angiitis that Dr. Szanto may have difficulty in classifying. These are in the category of but cannot be called periarteritis nodosa.

Dr. Szanto: Biopsy of a subcutaneous nodule was performed on the day prior to death, and, although the results were not available to the attending physicians, I should like to present the histological findings for Dr. Zimmerman's consideration. Sections revealed moderate infiltration of the deeper part of the corium by acute and chronic inflammatory cells, increasing in severity toward the subcutaneous fat tissue. The central portion of the subcutaneous nodule was composed of fat cells, shadowy in character, with basophilic granular precipitate interpreted as calcium deposit. A hemorrhagic zone containing foci of predominantly acute inflammatory cells surrounded the necrotic fat tissue. The appearance was that seen in pancreatic fat necrosis, namely preservation of the outline of the cells, with calcium deposit due to saponification of the fatty acids liberated from the necrotic fat cells (fig. 1, 2, and 3). Dr. Zimmerman, would this have made a difference in your final diagnosis?

Dr. Zimmerman: No further comment.

Clinical Diagnosis.—The clinical diagnosis was periarteritis nodosa.

Pathologist's Report

Dr. Szanto: At autopsy, innumerable small subcutaneous nodules were scattered over the chest, abdomen, and thighs, measuring up to 5 mm. in diameter. On cut section, these nodules were indurated, opaque, chalky, and pale yellow. Microscopically, they showed the same changes as were found in the biopsy specimen (fig. 4). The knees, ankles, shoulders, elbows, and right metacarpophalangeal joints were swollen. The skin over the involved joints was dusky-red. The joints contained cloudy, but not purulent, fluid which on direct smears contained numerous gram-negative bacteria. Cultures of the fluid aspirated at autopsy revealed Pseudomonas aeruginosa and Escherichia coli. Histologically, the synovial membranes were heavily infiltrated with acute and chronic inflammatory cells. The periarticular fat tissues showed fat necrosis surrounded by a zone of leukocytic inflammatory reaction, as has been seen in the pancreas and in the subcutaneous fat tissue. Some of the veins contained recent thrombi. The blood vessels in the perisynovial tissue were normal except for venous thromboses adjacent to areas of fat necrosis.

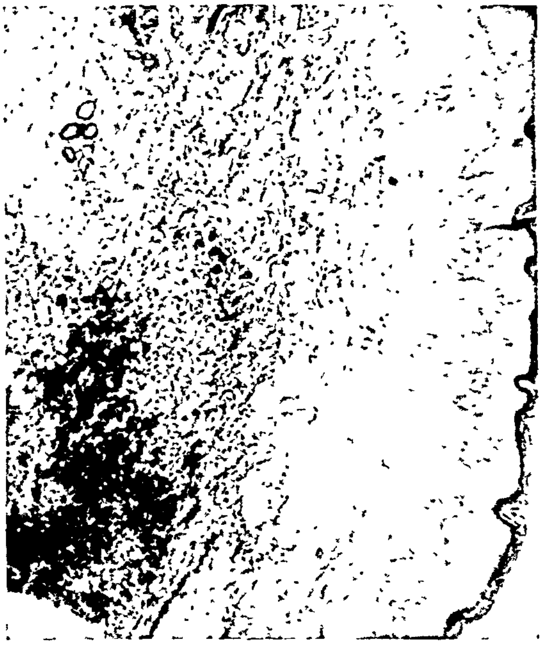

Fig. 1.—Photomicrograph of biopsy specimen from skin and subcutaneous nodule showing hemorrhage and acute inflammatory cells in deeper part of corium.

The abdomen was protuberant, and the peritoneal cavity contained 1,500 cc. of fluid with fibrin flecks. The right pleural cavity contained 400 cc. and the left 300 cc. of cloudy orange fluid. The pleural surfaces of the diaphragm were injected. The parietal peritoneum was of smooth, shiny appearance. A large, hemorrhagic, partly chalky, mesenteric mass extended downward from the pancreas to 9 cm. above the pubis. This mass was entirely within the mesentery (fig. 5). The peritoneal surface over the mesenteric mass was injected and flecked with yellow opaque foci. The transverse colon was attached to this mass by fibrinous adhesions which could be separated readily. The hepatic flexure was firmly adherent to the necrotic mesenteric mass.

The body and tail of the pancreas were well preserved, but the head of the pancreas was firm and contiguous with the mesenteric mass. The cut section of both was variegated, with hemorrhagic and chalky areas of fat necrosis. The pancreatic duct was moderately dilated and opened adjacent to, but separate from, the common bile duct. There was no evidence of cholecystitis or cholelithiasis. The gross findings suggested chronic pancreatitis on which there was recently superimposed an acute fat necrosis. Histologically, the entire pancreas showed interlobular and intralobular fibrosis and proliferating pancreatic ducts, confirming the gross pathological diagnosis of chronic pancreatitis. In addition, there was superimposed extensive pancreatic fat necrosis characterized by shadowy fat cells, calcification, and intravascular thrombus formation, more in the head, but also focally throughout the body and tail of the pancreas. The large mesenteric mass, as well as the retroperitoneal fat tissue, showed the same type of fat necrosis, hemorrhages, and vascular thromboses.

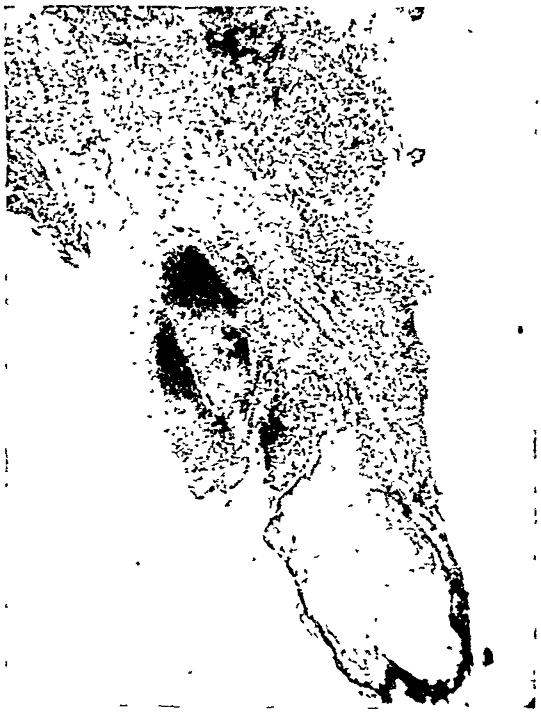

Fig. 2.—Subcutaneous part of biopsy specimen in figure 1 showing necrotic fat tissue and adjacent inflammatory reaction and hemorrhage.

Microscopically, the liver (1,500 Gm.) showed fatty changes, moderately enlarged portal fields, and focal necroses. Occasional bile casts were seen. The heart, myocardium, and subepicardial fat tissues were normal. A few atheromatous plaques appeared excavated and showed shadowy cells as seen in the areas of fat necrosis. The left lower lobe of the lung contained multiple, large, hemorrhagic infarcts and bronchopneumonic consolidation. Near the infarcts, many of the medium-sized branches of the pulmonary artery were completely occluded by recent thrombi. In the spleen, lipid-containing cells around the Malphigian corpuscles were seen. Some showed the ghost-like character seen in the necrotic fat tissue elsewhere. The fatty bone marrow showed no evidence of fat necrosis. The gastrointestinal tract and kidneys were normal. There was no evidence of prostatitis, epididymitis, or posterior urethritis. The testicles were atrophic. The central nervous system was grossly normal. Some of the sections revealed small foci of perivascular demyelinization in the white matter of the cerebrum and moderate oligodendroglia reaction.

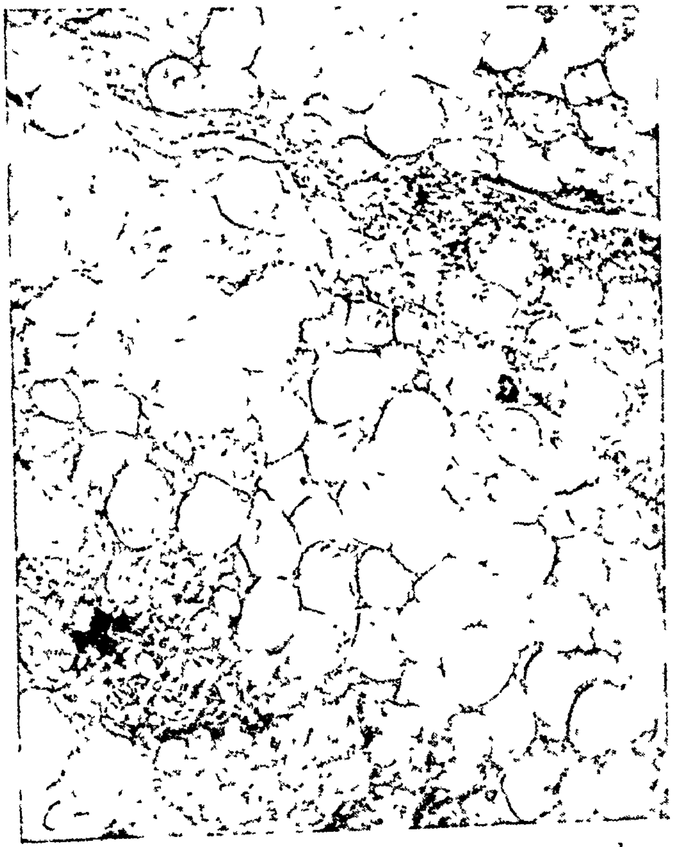

Fig. 3.—High power view of portion of specimen showing shadowy necrotic fat cells within nodule.

Pathological Diagnosis.—The pathological diagnosis was chronic relapsing pancreatitis with superimposed massive acute pancreatic fat necrosis, involving the head of the pancreas, and the retroperitoneal, mesenteric, periarticular, and subcutaneous fat tissue; toxic hepatitis; multiple pulmonary infarcts; and bronchopneumonia.

Comment

Dr. Szanto: The morphologic changes in the subcutaneous nodules in this case differ from the systemic nodular nonsuppurative panniculitis (Christian-Weber disease). The latter is characterized by preservation of the fat cells, infiltrated by relatively few acute and chronic inflammatory cells in the early stage, and progressive increase of the inflammatory reaction with replacement of fat cells by foam cells as the disease progresses. In our case, the subcutaneous nodules consisted of ghost-like fat cells with dystrophic calcification, perifocal inflammatory reaction, and hemorrhages. Involvement of the extrapancreatic fat tissues due to liberation of lipase from the pancreas occurs quite frequently in the course of acute pancreatitis.

Table 2 summarizes the previously reported sites of extrapancreatic fat necrosis, compared with those seen in this case. The frequency of involvement of the mesenteric fat tissue is well known. Less well known is the incidence of involvement of the mediastinal, subepicardial, and retroperitoneal fat tissue.[1] Fat necrosis of the subcutaneous fat tissue was described by Balser[2] in 1882, and similar reports[3] also appeared later. Involvement of the bone marrow is not at all rare[4] and has been produced experimentally by intravenous injection of lipase. Perivascular demyelinization of the white matter of the cerebrum associated with oligodendroglia reaction can also be ascribed to circulating lipase.[5] These alterations of the central nervous system may account for the confusion and semiconscious state of the patient. Involvement of the periarticular fat tissue with resulting severe polyarthritis, to our knowledge, has not been previously reported.

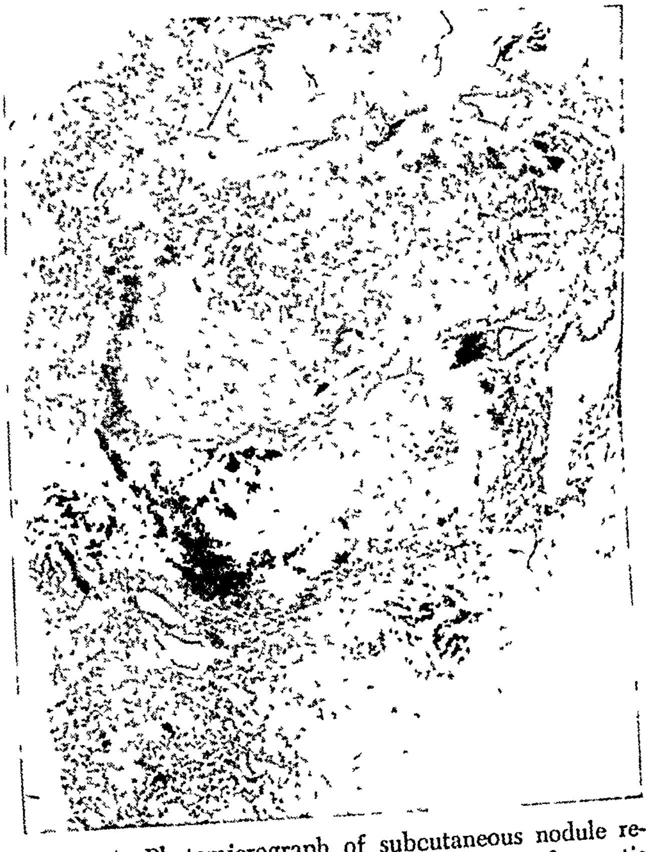

Fig. 4.—Photomicrograph of subcutaneous nodule removed at autopsy. Center of nodule consists of necrotic fat tissue with ghost-like fat cells surrounded by zone of inflammatory cells.

The interesting feature of this case was the onset, with polyarthritis followed by the appearance of disseminated subcutaneous nodules, while the abdominal symptoms appeared later. The involvement of the pancreas proper, revealed at autopsy, was not too extensive; it is possible that extrapancreatic involvement occurred early and was limited to the retroperitoneal space, enabling the escape of pancreatic lipase into the circulation by way of the lymphatics, circumventing the enterohepatic circulation. The resultant high lipase levels may account for the extensive involvement of the joints and skin.

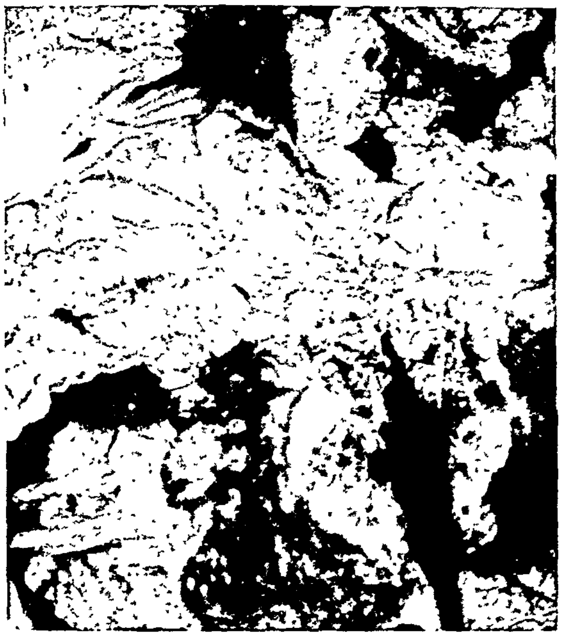

Fig. 5.—Relatively well-preserved body and tail of pancreas. Large hemorrhagic, chalky, mesenteric mass extends downward from pancreas.

The various theories about the etiology and pathogenesis of acute pancreatitis are summarized in table 3. An interesting recent theory[6] relates acute pancreatitis to the Schwartzman phenomenon, whereby intradermal injection of a cell-free filtrate of Salmonella, followed by intravenous injection of the same filtrate, results in hemorrhagic necrosis at the site of the original intradermal injection. Using this principle, injection of a bacterial endotoxin in sublethal doses into a pancreatic duct, with a subsequent provocative intravenous injection of the same endotoxin, has produced a fulminating pancreatitis in rabbits. Any substance with antigenic properties may cause a Schwartzman reaction, and antigenic specificity is not involved, i. e., the provocative antigen need not be identical with the sensitizing antigen.

TABLE 2.—*Sites of Extrapancreatic Fat Necrosis*

Site	In Literature	In Our Case
Mesenteric fat tissue	+	+
Retroperitoneal fat tissue	+	+
Mediastinal fat tissue	+	−
Subepicardial fat tissue	+	−
Subcutaneous fat tissue	+	+
Bone marrow	+	−
Central nervous system (perivascular demyelinization)	+	+
Periarticular fat tissue	−	+

It may be recalled that, in the case under discussion, the joint involvement was conspicuous early in the course of the disease. There was no definite evidence of rheumatoid arthritis, either clinically or pathologically. Bacterial polyarthritis, specifically of gonorrheal origin, should be considered, although a most careful search failed to reveal any evidence for a gonorrheal infection of the genital organs. Gonorrheal polyarthritis in the early stages shows a serous type of synovitis, and cultures of synovial fluid may be negative.

The association of polyarthritis with periarticular fat necrosis and pancreatic fat necrosis raises the following possibilities: 1. There may have been a pure coincidence of a rheumatoid polyarthritis with pancreatic fat necrosis, whereby the periarticular fat necrosis occurred in a site of decreased resistance; but, despite the high incidence of rheumatoid arthritis and the relative frequency of pancreatitis, such a coincidence of these with periarticular fat necrosis has never been reported. 2. The pancreatic fat necrosis in the early clinically latent phase of the disease, with liberation of lipase into the circulating blood, may have led to a chemical polyarthritis due to extensive periarticular fat necrosis. 3. A bacterial (gonorrheal?) polyarthritis preceding pancreatitis cannot be excluded, despite the negative bacteriologic findings.

TABLE 3.—*Etiology of Acute Pancreatitis**

- I. The common channel theory: reflux of bile into pancreatic duct secondary to obstruction of ampulla of Vater
  - a. Calculus at ampulla of Vater
  - b. Spasm of the sphincter of Oddi
  - c. Edema
- II. Obstruction of pancreatic ducts by
  - 1. Stone
  - 2. Spasm of sphincter of ampulla of Vater
  - 3. Edema of papilla of Vater
  - 4. Tumor of pancreas
  - 5. Squamous metaplasia of the epithelium in the ducts
  - 6. Surgical ligature
- III. Alcohol
  - A. Acute
  - B. Nutritional
- IV. Metabolic disturbances
  - 1. Malnutrition (as it has been produced experimentally by ethionine)
  - 2. Hyperlipemia
- V. Trauma
- VI. Vascular changes
  - (Necrotizing arteriolitis; periarteritis nodosa)
- VII. Infection
  - (e. g. mumps, septicemic, acute cholecystitis?)
- VIII. Allergic
  - a. Schwartzman phenomenon

* Richman[7] (modified).

One might speculate, on the basis of morphologic evidence of a chronic pancreatitis, that the pancreas was already sensitized. A bacterial polyarthritis could then have provided an antigenic provocation for a Schwartzman phenomenon, which led to an acute pancreatic fat necrosis, in the course of which large amounts of circulating trypsin and lipase were liberated. The circulating lipase caused a periarticular fat necrosis, which in turn caused a progression of the polyarthritis, despite the fact that the bacteria, as such, responded to the antibiotics, i. e., a transformation of the original bacterial arthritis into a chemical arthritis occurred. If the nodules were originally situated only in the skin (as clinically described) and only later appeared in the subcutaneous fat tissue (as described in the biopsy specimen and at autopsy), one could postulate that originally circulating trypsin caused vascular alterations in the deeper layer of the corium, with resultant skin nodules, and later the circulating lipase resulted in subcutaneous fat necrosis and subcutaneous nodules.

Summary

A chronic alcoholic patient had episodes of abdominal pain for two years, on the basis of a relapsing pancreatitis. Four weeks prior to his death, he developed swelling and tenderness of the various joints, with chills and fever. This could have been due to a bacterial polyarthritis associated with an acute pulmonary lesion such as pneumonia. The bacterial infection could have precipitated an acute pancreatic fat necrosis, on the basis of a Schwartzman phenomenon. Excessive amounts of circulating enzymes (trypsin and lipase) caused a striking involvement of the extrapancreatic fat tissue, cutaneous and subcutaneous nodules of fat necrosis, and necrosis of the periarticular fat tissue, initiating a chemical polyarthritis. The abdominal symptoms that appeared later were due to extensive mesenteric fat necrosis. The terminal jaundice was due to hepatocellular damage (toxic hepatitis) secondary to the pancreatic and extrapancreatic fat necrosis. The depression of blood calcium level was characteristic for extensive pancreatic fat necrosis and was due to saponification of the fatty acids liberated from neutral fat by the enzymatic action of pancreatic lipase.

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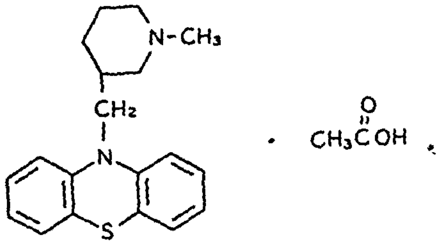
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. Kautz, M.D., *Secretary.*

Mepazine Acetate.—10-[(1-Methyl-3-piperidyl) methyl]phenothiazine acetate.—The structural formula of mepazine acetate may be represented as follows:



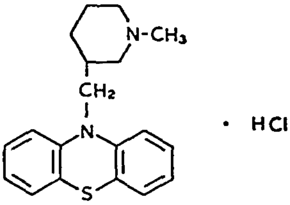
Actions and Uses.—Mepazine acetate has the same actions and uses as mepazine hydrochloride, except that it is administered parenterally. (See the monograph on mepazine hydrochloride.)

Dosage.—Mepazine acetate is administered by intramuscular or intravenous injection. For severely agitated psychotic patients, the dose by either route is 50 mg. three or four times daily. For the treatment of severe nausea and vomiting, daily doses of 25 to 75 mg. are injected intramuscularly. Dosage for use in surgical and obstetric patients has not been firmly established, but single intramuscular or intravenous doses ranging from 50 to 200 mg. or more have been employed.

Mepazine acetate may be injected parenterally either as the full-strength solution or as a diluted solution. Chloride or alkaline solutions should not be used as diluents since they cause precipitation of mepazine acetate. Oral therapy with the hydrochloride salt should be substituted for parenteral injection as soon as possible.

Preparations: solution (injection) 50 mg. in 2 cc.
Applicable commercial name: Pacatal Acetate.

Mepazine Hydrochloride. — 10-[(1-Methyl-3-piperidyl)methyl]phenothiazine hydrochloride.—The structural formula of mepazine hydrochloride may be represented as follows:



Actions and Uses.—Mepazine hydrochloride is a phenothiazine derivative with actions and uses similar to, but not identical with, those of chlorpromazine. Although less potent, mepazine is not merely a weak chlorpromazine. Pharmacological studies indicate that it differs from chlorpromazine in that it does not lower the body temperature in rats as does chlorpromazine; it does not antagonize the waltzing syndrome in mice as does chlorpromazine; and it augments carotid sinus reflexes in cats whereas chlorpromazine inhibits them. The significance of these differences with respect to its clinical usefulness is, at present, unclear. The drug is used principally for its calming or tranquilizing action in the management of neuroses and psychoses in which anxiety, tension, agitation, and increased psychomotor activity are predominant; it is said to exert a selective action to normalize the thinking process of mentally or emotionally disturbed patients. Because mepazine is less potent than chlorpromazine, it does not produce the excessive sedation, drowsiness, and depression which frequently accompany therapy with the latter drug. On the other hand, the diminished potency of mepazine makes it less effective than chlorpromazine for the long-term control of the most severe forms of agitation and tension; it has little or no immediate effect on acute psychotic disturbances. In terms of over-all psychotherapeutic effectiveness, mepazine might be considered to be intermediate between the most potent agents such as chlorpromazine and the milder agents such as meprobamate.

Like chlorpromazine and other phenothiazine derivatives, mepazine hydrochloride exerts an antiemetic effect and may be used for the control of nausea and vomiting from a variety of causes. The drug has also been used for its calming effects in surgery, in obstetrics, and in anesthesia. Other reported clinical applications include use in narcotic withdrawal to control restlessness and agitation, in chronic alcoholism to lessen anxiety and tensions, and in advanced neoplastic states to reduce the quantity of narcotics needed for control of pain. However, sufficient evidence is not available to establish its usefulness for the latter purposes.

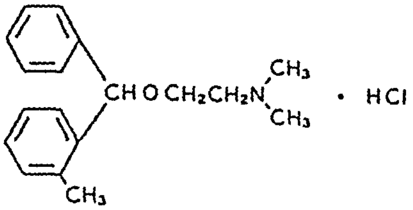
The acute toxicity of mepazine hydrochloride in experimental animals is less than that of chlorpromazine hydrochloride, and, in general, its clinical use is followed by a somewhat lower incidence of side-effects and untoward reactions. As already indicated, the usual doses produce a calming effect, with little sedation and drowsiness. Although jaundice has not as yet been observed with administration of mepazine, physicians should be alert to its possible occurrence. The drug should not be given to patients with a history of jaundice or liver damage. The most frequent side-effects of mepazine are atropine-like in nature and include blurring of vision, dryness of the mouth, and constipation. Since constipation can lead to more serious forms of intestinal obstruction, it should not be neglected; if necessary, laxatives should be prescribed. Less frequent side-effects include occasional dizziness, tremor, urinary retention, and transient hypotension. The most serious toxic reaction to mepazine is referable to hematopoietic depression. As with chlorpromazine, the drug can produce leukopenia and granulocytopenia. It should, therefore, be used with discretion; peripheral blood cell counts are indicated at frequent intervals during therapy, and patients should be advised to report to the physician immediately upon the onset of fever, sore throat, or marked weakness. Because it potentiates the action of other central nervous system depressants, mepazine is contraindicated in patients under the influence of large doses of narcotics, barbiturates, or unknown large quantities of alcohol.

Dosage.—Mepazine hydrochloride is administered orally. For the treatment of ambulatory neurotic patients, the usual initial dose is 25 mg. three or four times daily. This dosage can be increased every week by increments of 25 mg. per day until the desired effect has been attained. For those psychiatric conditions which are severe enough to require hospitalization of the patient, the initial dose is 100 mg. per day; this may be increased by 50 mg. every five to seven days. Maintenance dosage for such patients is usually 400 mg. per day or more.

For the treatment of nausea and vomiting, the dosage ranges from 50 to 100 mg. per day. Dosage for use in surgical and obstetric patients has not been firmly established; single doses ranging from 50 to 200 mg. or more have been employed.

Preparations: tablets 25, 50, and 100 mg.
Applicable commercial name: Pacatal Hydrochloride.

Orphenadrine Hydrochloride.—N,N-Dimethyl-2-(*o*-methyl-α-phenylbenzyloxy) ethylamine hydrochloride.—The structural formula of orphenadrine hydrochloride may be represented as follows:



Actions and Uses.—Orphenadrine hydrochloride, the *o*-methyl analogue of the antihistamine, diphenhydramine hydrochloride, produces a reduction of voluntary muscle spasm. The effect is central, presumably by an inhibitory action on cerebral motor areas, and resembles the central effects of atropine. Orphenadrine exerts only weak antihistaminic and sedative effects. It is not primarily a peripherally acting anticholinergic agent since, in therapeutic doses, it produces few of the typical effects on smooth muscle, the eye, or secretory glands which characterize atropine and other peripheral parasympathetic blocking agents. The skeletal muscle relaxation is not of the type produced by mephenesin or zoxazolamine, since there is no evidence that it interrupts transmission through peripheral neuromuscular pathways. Nor is there any indication that it acts at the myoneural junction in the manner of the curariform drugs; it does not cause ganglionic blockade.

Orphenadrine has been used for the symptomatic management of paralysis agitans (Parkinson's disease). Subjective observations seem to indicate that the drug may bring about beneficial effects in approximately half of the patients so treated. Rigidity is apparently relieved much more readily than is tremor; in occasional patients with severe spasticity, tremor may even be accentuated as the spasticity is relieved. Other salutary effects ascribed to the action of the drug include relief of oculogyria, sialorrhea, diaphoresis, blepharospasm, and disturbances in gait and balance. The drug also exerts a euphoriant effect which is useful in combating the depression and fatigue that frequently accompany this syndrome. In common with other antiparkinsonian drugs, the therapeutic effectiveness of orphenadrine diminishes with prolonged use. For this reason, and because it is considered somewhat less active than other antiparkinsonian drugs, orphenadrine is probably best employed as an adjunct to such other agents as procyclidine, trihexyphenidyl, cycrimine, or benztropine for the treatment of paralysis agitans. It may, however, be tried alone for patients who have become refractory to the other antiparkinsonian drugs.

Because of its antispastic effect on voluntary muscle, orphenadrine has been proposed for use in a variety of clinical conditions which may be unrelated in etiology but in which pain due to skeletal muscle spasm is present. These have been described as sprains, strains, fibrositis, whiplash injuries, noninflammatory rheumatic and arthritic states, and torticollis. Although such use might be considered a logical clinical application of the drug's pharmacological action, the evidence available to date is not adequate to permit a sound conclusion as to the ultimate effectiveness of such therapy. Further studies are also needed to confirm the possible usefulness of orphenadrine in the treatment of the extrapyramidal involvement associated with high doses of reserpine or phenothiazine-type tranquilizing agents.

The clinical toxicity of orphenadrine hydrochloride appears to be low, at least with therapeutic doses. Thus far, side-effects have been limited to nausea, dryness of the mouth, dizziness, mild excitation, and occasional hallucinations. Most of these effects tend to subside or disappear with a reduction in dosage. Because of its anticholinergic classification, orphenadrine should be administered cautiously to patients with glaucoma, tachycardia, or urinary retention.

Dosage.—Orphenadrine hydrochloride is administered orally. The usual initial dose is 50 mg. given three times a day. This dosage should then be adjusted according to the clinical response of the individual patient and the appearance of side-effects.

Preparations: tablets 50 mg.

Applicable commercial name: Disipal.

Riker Laboratories, Inc., coöperated by furnishing scientific data to aid in the evaluation of orphenadrine hydrochloride.

Pancreatic Dornase.—A stabilized preparation of the enzyme, deoxyribonuclease, prepared by fractional precipitation of aqueous acid extracts of beef pancreas followed by dialysis, sterilization by filtration, and lyophilization. The activity of pancreatic dornase is determined by measuring the rate at which it reduces the viscosity of thymus deoxyribonucleic acid, potency being expressed in terms of units. One unit is an amount of enzyme which causes a drop of one viscosity unit in 10 minutes at 30 C, where the flow-time of water is taken as one viscosity unit.

Actions and Uses.—Pancreatic dornase is derived from beef pancreas, and, in contrast to the deoxyribonucleases produced by hemolytic streptococci (streptodornase), it is a single nuclease. Like streptodornase, it acts directly upon a substrate of deoxyribonucleoprotein (and deoxyribonucleic acid). The action of pancreatic dornase has been characterized as one of rapid depolymerization, with a resulting decrease in viscosity of purulent material. Pancreatic dornase degrades deoxyribonucleoprotein to relatively large-sized fragments, thus differing from streptodornase, which continues this degradation through to free purine and pyrimidine compounds. Pancreatic dornase acts only on extracellular accumulations and disintegrating cells but not on living material. Enzymatic degradation is completed within the first few minutes of contact with the substrate.

Inhalation therapy with aerosols of pancreatic dornase has been employed to reduce the tenacity of pulmonary secretions and to facilitate the expectoration of sputum in certain bronchopulmonary infections in which thick mucopurulent secretions, particularly mucopurulent plugs, are present. On the basis of purely subjective observations, it is the clinical impression of most investigators that inhalation therapy with pancreatic dornase definitely benefits patients with purulent tracheobronchitis, bronchiectasis, abscesses, atelectasis, unresolved pneumonia, chronic bronchial asthma, and emphysema in which tenacious pulmonary secretions are a complicating factor. In a sizable percentage of such patients, clinical improvement is manifested by a change in the character of the sputum from a thick, gelatinous consistency to a thin, milky material which may be raised more easily. Part of the beneficial action of pancreatic dornase in the foregoing conditions has been ascribed to an ability of the enzyme to allow concomitantly administered antibiotics to reach the area of infection more readily. Thus far there is inadequate experimental evidence to support this view. The use of the drug as an adjunct in obtaining bronchial secretions and cellular debris for cytological study in patients with suspected bronchogenic carcinoma must be considered experimental.

The clinical toxicity of pancreatic dornase appears to be minimal, and aerosols of the drug are better tolerated than similar aerosols of crystalline trypsin. From experience to date, it would appear that allergic phenomena do not constitute a serious problem. Nevertheless, sensitivity to beef protein should be kept in mind; a few reported cases of dyspnea and generalized hypersensitivity reactions suggest that allergy can occur after prolonged use. More experience is needed to determine the ultimate sensitizing potential of pancreatic dornase.

Dosage.—Pancreatic dornase is administered by inhalation. The freeze-dried powder of purified enzyme should be reconstituted with 2 cc. of sterile isotonic solution of sodium chloride immediately prior to use. Best results are reported when the drug is administered as an aerosol, either a direct nebulizer-oxygen tank arrangement or an intermittent positive-pressure breathing apparatus being used. When the latter method is employed, more complete ventilation of the lung and better distribution of the enzyme take place. It is questionable whether the use of ordinary hand atomizers or nebulizers is an effective method of treatment.

For the treatment of bronchopulmonary infections, the suggested dosage is 50,000 to 100,000 units once to three times daily for a period of two to six days, until improvement occurs and the maximal response is obtained. Treatment may be repeated after an interval of a few days or when clinical symptoms indicate further need of therapy. For use as an adjunct in obtaining specimens of bronchial secretions and cellular debris for cytological study, the proposed dose is 100,000 units given as a single dose prior to bronchoscopy, or treatment may be continued over a period of days.

Preparations: powder (inhalant) 100,000 units with 2 cc. of sterile diluent.

Applicable commercial name: Dornavac.

Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of pancreatic dornase.

Intramuscular Use of Crystalline Trypsin in Pulmonary Diseases

The Council has evaluated the available evidence for the use of intramuscularly administered aqueous solutions or oil suspensions of crystalline trypsin (Parenzyme) as an adjunct to the treatment of severe bronchopulmonary diseases, which are characterized by tenacious secretions not susceptible to the action of expectorants. Included among such conditions are bronchial asthma, emphysema, and bronchiectasis. The enzyme is intended to reduce the viscosity and, hence, to facilitate the expectoration of thick, mucopurulent, pulmonary secretions, particularly inspissated mucopurulent plugs.

The available evidence for the intramuscular use of the drug for the foregoing types of pulmonary disease constituted a small number of case reports on patients in whom some improvement was observed on the basis of x-ray changes, increased vital capacity, lessened respiratory embarrassment, and ease with which the sputum was raised. Since the case histories were uncontrolled, the criteria used to demonstrate improvements may not be reliable. In a number of case histories the concomitant use of antibiotics complicated the evaluation of trypsin for bronchial pulmonary diseases. Hence, the Council concluded that its usefulness for pulmonary diseases has not as yet been fully established by the evidence so far available.

The usual doses for intramuscular injection of crystalline trypsin vary from 2.5 to 5 mg. one to four times daily for a period of three to eight days. Dosage must be individualized depending on the severity of symptoms and the degree of response. Adequate precautions against accidental intravenous injection should be exercised.

The Council voted to amend New and Nonofficial Drugs accordingly to describe the intramuscular use of crystalline trypsin in pulmonary disease.

The National Drug Company cooperated by furnishing scientific data to aid in the evaluation of this additional use of crystalline trypsin.

COUNCIL ON INDUSTRIAL HEALTH

OCCUPATIONAL DERMATOSES—AN INTRODUCTION

This is the first in a series of reports prepared by the Committee on Occupational Dermatoses of the Council on Industrial Health, American Medical Association.

B. DIXON HOLLAND, M.D., *Secretary.*

It is reasonable to assume that occupational skin diseases are as old as civilization. The medical literature of the early 16th century recorded occupational dermatoses among metal workers, miners, and miscellaneous artisans. Incidental references to trade dermatoses were chiefly of academic interest, however, until the development of workmen's compensation laws transferred to employers the economic problem involved in occupational dermatoses. This occurred in the United States after 1911 and chiefly in the last quarter-century.

Industrial dermatoses are more than ever a product of our present industrial age, with its intensified technical development and the ever-increasing scope of workmen's compensation laws. Several factors have helped to control or reduce the incidence of industrial dermatoses, including improved personal hygiene, a better understanding of the nature of contact dermatoses, better training of industrial workers, modern engineering, more effective plant supervision, and improved plant facilities. Somewhat offsetting these improvements are the increased number of workers engaged in industrial pursuits and the more widespread use of chemical processes. Further, the constant introduction of new chemicals has increased the sources of dermatoses, particularly those incidental to contact with plastics (synthetic resins), petroleum products, and synthetic materials from petroleum and coal tar. We may, therefore, anticipate that industrial dermatoses will continue to be an important problem in industrial medicine.

Statistics on this subject are important chiefly to give the uninitiated an idea of the scope and importance of the problem; however, statistical information is quite limited. In many states statistics are available only on the basis of compensation paid for disability, and, since a large proportion of cases of occupational dermatoses are nondisabling, compensation figures do not provide an accurate indication of incidence. Available information, obtained from widely scattered localities and diverse industries, indicates a significantly high incidence of industrial dermatoses.

For example, Schwartz,[1] of the U. S. Public Health Service, basing his reports on an extensive nationwide investigation of a variety of industries, estimated that approximately 1% of industrial workers are affected with some form of occupational dermatosis at any given time. He observed that, in the United States, occupational dermatoses comprise about two-thirds of all occupational diseases for which compensation is paid. In another study, made in 1951, occupational disease statistics gathered by the U. S. Public Health Service from 28 states showed that dermatoses constituted approximately 55% of all occupational diseases reported.[2] Other investigators have noted that industrial dermatoses usually comprise from 30 to 40% of the occupational diseases reported. The incidence of dermatoses of industrial origin observed by dermatologists in private practice in metropolitan areas has varied from 5 to 20% according to the nature and locality of practice. In the decade ending in 1940, a conservative estimate of the over-all cost of occupational dermatoses in the United States was placed in excess of 100 million dollars in an average year. Although no accurate cost analysis of these diseases has been made for the present time, the marked change in the national economy serves to indicate that a present estimate would amount to well over 150 million to 200 million dollars in an average year.

These figures emphasize the importance of occupational dermatoses and point up the necessity of an adequate knowledge of dermatology on the part of physicians engaged in the practice of industrial medicine. In addition, they indicate the need of knowledge on the part of the dermatologist concerning the nature and hazards of occupational activities in relation to their effects on the skin.

Patients with dermatoses possibly of occupational origin are seen by the dermatologist chiefly when referred by industrial physicians, industrial nurses, employers, and insurance carriers. In the experience of members of this Committee, some 30 to 40% of the cases are ultimately determined to be nonoccupational in origin. This emphasizes the importance of sound dermatological judgment in appraising and diagnosing such cases.

The members of the Committee on Occupational Dermatoses are Drs. Donald J. Birmingham (Chairman), Cincinnati; Leonard Weber (Secretary), Chicago; Frank C. Combes, New York; A. Fletcher Hall, Santa Monica, Calif.; James W. Jordan, Buffalo; George Morris, Boston; and Ray O. Noojin, Birmingham, Ala.

Industrial dermatoses comprise those occupationally acquired diseases of the skin caused by chemicals, physical agents, mechanical factors, bacteria and fungi, animal parasites, plants, and woods (and occupational cancer). It is estimated that about 90% of all occupational dermatoses observed in industrialized areas, excluding mechanical injuries, are of chemical origin. In general, cases of dermatitis due to chemicals are also of greater importance because of their severity, difficulty of management, and frequently disabling character.

Of the cases of contact dermatitis, approximately 80% are caused by primary irritants, for example, organic and inorganic acids and alkalies, corrosive salts, reducing agents, petroleum oils, solvents, tar, and pitch. Approximately 20% of occupational dermatoses are caused by sensitizing agents. The latter group is highly important because of the more obscure character of the disease, the greater difficulty in diagnosis and management, and the tendency for it to recur or to run a prolonged course. The dermatoses due to sensitizers, particularly, require experienced dermatological knowledge for correct diagnosis and successful management. The sensitizing agents include dye intermediates, dyes, natural and synthetic resins and waxes, bichromates, rubber compounds, accelerators, photosensitizers, and explosives. Some sensitizing chemicals, in more concentrated form, may also act as primary irritants.

In any search for the cause of an occupational dermatitis, it is just as important to check on the skin cleansers used at work as to investigate the contacts peculiar to the industry. The possibility of secondary employment should not be overlooked. In addition, other activities outside of the work environment, such as hobbies and work around the home, must be considered, since these may produce a dermatitis identical with that resulting from industrial exposures. In such investigations, especially of dermatoses suspected of having been caused by sensitizing agents, the patch test is particularly important as a diagnostic aid.[3] The use of preemployment patch tests is discouraged because workers are not likely to show positive reactions to sensitizing agents before they come in repeated contact with them, and when such tests are negative a false sense of security can be created.

It is possible to reduce materially the incidence of primary irritant dermatitis by education of employees and improvement in plant operations and procedures. The handling and correction of allergic or sensitization dermatoses is more difficult. It requires more careful selection of employees in hazardous industries, greater effort in the education of workers, prompt and efficient dermatological care of those who develop dermatitis, and, if practicable, replacement of the sensitizer by a nonsensitizing material. Prompt improvement and early recovery usually follow removal from contact with the suspected causative occupational agent and appropriate treatment. When this does not occur, suspicion should be directed to a probable nonoccupational cause or to the factors which are known to prolong contact dermatitis.

The predominant types of industrial dermatoses vary considerably in different localities in accordance with the types of industry. For example, in Boston chrome dermatitis is of importance because of the large number of employees in leather industries. In Milwaukee, cutting oils and solvents used in the machine industries cause the majority of industrial dermatoses. In Los Angeles, where the airplane industry employs large numbers of workers, dermatoses from plastics are commonly found.

It is axiomatic that any industrial or occupational activity may lead to the development of a dermatitis in a susceptible individual under certain circumstances and that dermatoses presenting a great variety of clinical appearances may have an occupational origin. However, with modern control measures the hazard of occupational dermatitis may be regarded as minimal and the prospect of prompt recovery as maximal in the majority of occupations, particularly when adequate nursing and medical care are available.

Summary

In summary, occupational diseases of the skin constitute the major portion of all compensated illness of industrial origin. Causes of occupational dermatoses are numerous, but the majority of these diseases result from contact with primary irritant chemicals. Allergy accounts for no more than 20% of the cases. The numerous contact agents in the occupational environment are associated with a wide variety of clinical lesions. Therefore, the successful handling of these cases requires a knowledge of plant operations and a reasonable degree of skill in dermatological diagnosis. Understanding the value of preventive measures lessens the incidence of occupational skin disease and also increases the chance of prompt recovery in the management of the occupational dermatoses.

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THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

EXPECTORANTS

GUEST EDITORIAL

Harry Beckman, M.D.

MOST MEN who have given thought to the term "expectorants" as drugs used for the purpose of increasing the respiratory tract fluid would agree that the term is unfortunate, since there is in it the implication that the effectiveness of such drugs can be measured in terms of the sputum produced. This is what Alstead[1] (1941) considered that he had done when he pronounced ammonium chloride ineffective as an expectorant because it had not increased expectoration. But when Holinger, Basch, and Poncher[2] (1941) collected respiratory tract fluid by means of postural drainage and bronchoscopic suction they found that the expectorant drugs liquefy the respiratory tract fluid quite appreciably. Boyd[3] (1954) pointed out that indirect measurement of the action of expectorants upon respiratory tract fluid through evaluation of their therapeutic efficacy against cough has resulted only in divergent conclusions, as was to have been expected. In the first place, cough due to irritation of the pharynx cannot be relieved by expectorants because the respiratory tract fluid arises entirely from sources below this area. In the second place, one could certainly not expect t[illegible]influence irritations of the diaphragm and pleu[illegible] And in the third place, there are pharmacologica[illegible]gents that undoubtedly increase respiratory t[illegible]ct fluid but are nevertheless clinically unacceptable as expectorants for the treatment of cough because they produce their effects only at the cost of a prohibitive amount of side-reactions and toxicity. Nevertheless, there is some scientific evidence to support clinical impression of the value of drugs that increase respiratory tract fluids.

On the level of animal experimentation, in which respiratory tract fluid is collected quantitatively through a tracheal cannula under standardized conditions, ammonium chloride has been found to augment the output only if the gastric branches of the vagus are intact, indicating that this compound acts through irritation in the stomach. It is an old clinical favorite, despite the fact that it is disagreeable in taste and objectionably diuretic in some patients.

The iodides can also be shown to act through initiation of the gastric reflex. No experimental evidence of direct action on the bronchial glands exists, but it is nevertheless possible that some of the effect may result from partial respiratory tract excretion of iodide because the presence of iodine compounds in the fluid, reported by Tuft and Levin[4] (1942), was confirmed in animals by Boyd and associates[5] (1945).

Ipecac, which pediatricians often prefer to any other expectorant, appears definitely to act through the gastric reflex, but part of the expectorant action of this drug may be an expression of its potential emetic action (manifested on higher dosage) since increase in at least pharyngeal and salivary secretions is a part of nausea.

Banyai and Cadden[6] (1943) showed that carbon dioxide by inhalation not only stimulates the myoelastic structures of the lung and leads to forceful peristaltic movement of the bronchi but also, in man, has a directly exerted expectorant action through liquefying the mucopurulent inflammatory exudate that stagnates in the bronchial tract.

Inhalation of warm, moist air, as from the familiar steam kettle, appears to have a definite expectorant action through diluting the respiratory tract fluid, but it has not been shown experimentally that secretory production of the fluid is increased. However, when the water vapor inhaled is in the form

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of Alevaire (sterile aqueous solution of Superinone [oxyethylated tertiary octylphenol-formaldehyde polymer], in combination with glycerin and sodium bicarbonate), it is considered by many observers to be a true topically acting expectorant, as claimed by Tainter, Nachod, and Bird[7] (1955). Special techniques and equipment are required for the administration of this proprietary agent, but it seems to be finding considerable favorable use by inhalation in the treatment of exudative tracheobronchial and pulmonary diseases.

Boyd[8] (1946) found that, while cough syrups as such may have a buccopharyngeal demulcent and sialogogue (stimulation of salivary flow) effect, pharmacological action as expectorants cannot be demonstrated for them unless the syrup itself contains an expectorant such as tolu balsam or possibly licorice.

THE CASE OF THE DEADLY PARALLEL

Statistics can often be presented to the uninitiated in such a manner that they seem to prove something when in reality they prove nothing at all. Some years ago a statistical parallel was presented between the steadily increasing use of mechanical refrigeration and the rapidly rising death rate from cancer. More recently the growing cancer death rate has been presented in parallel with the upward trend in consumption of soft drinks. In each instance, the unwarranted conclusion was drawn that there was a cause and effect relationship in these statistical parallels.

In like manner, parallels of a nonstatistical nature can be used effectively to appear to prove what they do not prove at all. A renewed interest in physical fitness as a neglected phase of total fitness has brought forth many public expressions of viewpoints, often differing and sometimes conflicting. It has been suggested, not to say demanded, that the Presidential Council on Youth Fitness become in effect an operating agency, a super organization issuing standards, prescribing methodology, and in other ways usurping the established activities of professional agencies better equipped to deal with these questions than is any council of lay persons no matter how eminently qualified in their own fields.

Returning to the deadly parallel, *Sports Illustrated Magazine*, which has been demanding more action from the Council and which in its issue of May 26, 1958, deplored the alleged nonactivity of the Council, has now published in its issue of June 16 a further demand for action from the Council coupled with an alleged parallel. Under the picture of the Honorable Fred Seaton, Secretary of the Interior and Chairman of the President's Fitness Council, is a catchline suggesting that the Secretary "could take a 34-year-old cue" from former Secretary of Commerce Hoover, who in 1925 "brought order out of highway chaos" by presenting the Hoover Uniform Highway Code. The smiling picture of Mr. Hoover flanked by standardized road signs is shown under the picture of Secretary Seaton.

This parallel is as superficial as such a comparison could well be. The standardizing of road signs and traffic guides is a far cry from solving the human problem of personal fitness. A closer parallel would have been the equally unsolved problem of driver motivation to safe driving which sometimes seems as insoluble today as it was when Mr. Hoover codified highway safety regulations.

Sports Illustrated demands a statement from the Council on fitness tests. But such tests have already been suggested by the American Association for Health, Physical Education, and Recreation, after considerable research. Also, several states have done research and have tests of their own which they hope to implement. *Sports Illustrated* wishes also to have the Council prescribe essential activities to be included in physical education programs at various ages; minimum equipment for physical education programs; minimum educational requirements for physical educators; patterns for cooperation between recreation and physical education leaders; and—the editor says he can think of quite a few more.

Recommendations relating to all of these areas and many more have been fully covered by professional groups, and there is ample professional literature for the guidance of those who are interested on a professional level. There is no necessity for the Council to assume leadership in areas where adequate leadership already exists; many such areas are represented on the Citizens' Advisory Committee to the Council.

The medical profession has already expressed its interest in the President's program for better fitness. A representation of its membership sits on the Advisory Committee and has endeavored to function constructively in this relationship. Physicians as a whole support the objectives of an improved activity program for Americans at all ages as an important facet, but not the whole, of a program for better total fitness. Doctors, however, are strong believers in free private enterprise and are unwilling to enlarge the functions of federal governments. They believe in cooperation on a voluntary basis and will go much further with any movement which is based on such a philosophy than with a federally centered, bureaucratically directed movement.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Whether you see the House of Delegates in operation for the first time or for the 32nd as I have, you immediately are impressed with the democratic manner and atmosphere in which it functions.

Last month in San Francisco our policy-makers held their first 1958 session. Seldom have I seen the floor debate so stimulating and the discussions in reference committees so intense. Sixty-three resolutions were introduced and the pros and cons were heard on every issue.

For example, on the matter of relations between medicine and the UMWA Welfare and Retirement Fund the House preferred not to accept the reference committee report. This report concurred with the Board of Trustees' recommendation that an educational campaign concerning the benefits of free choice of physicians and hospitals be deferred until the December report of the Commission on Medical Care Plans. The vote on the amended report was 110 to 72 in favor of immediate action.

As I emphasized in my report to the House, "the A. M. A. accepts the need for experimentation in new methods of financing medical care. It is ready, willing and anxious to cooperate with labor and all other groups honestly attempting to solve health problems. But the medical profession will not abandon or compromise its basic position on free choice of physician by the patient, or on keeping the doctor-patient relationship unviolated by third-party interference."

The House again supported the principal voluntary health agencies and their individual programs of research, public and professional education, and fund-raising in their particular spheres of interest.

In the interest of federal economy the House urged congressional action to restrict VA hospitalization of veterans to those with service-connected disabilities. This latest action on the VA issue was taken because the federal government in 1957 spent more than 600 million dollars on medical care of veterans in VA hospitals and because about 75% of these hospitalized veterans had non-service-connected disabilities.

On the federal Medicare issue the House reaffirmed the Association's basic contention that Medicare does not require fixed fee schedules. It also said that the establishment of such schedules would be more expensive than permitting physicians to charge their normal fees.

Your House approved a Council on Mental Health report on the "Medical Use of Hypnosis," which states that general practitioners, medical specialists, and dentists might find hypnosis valuable as a therapeutic adjunct within the specific field of their professional competence.

It also recommended that the A. M. A. join with other interested groups in setting up an expanded voluntary program to seek elimination of objectionable advertising of over-the-counter medicines; asked that a Committee on Atomic Medicine and Ionizing Radiation be appointed and that it inform the public on all phases of radiation hazards related to health; and recommended that general hospitals —wherever feasible—be encouraged to permit the hospitalization of suitable psychiatric patients.

At the opening session of the House I commented that "medicine today is more alert than ever before to changing times and new demands, and that it needs the greatest possible wisdom to adapt medicine's finest ethics and traditions to the modern framework of medical economics."

By its actions and decisions the House has shown its awareness and alertness to modern-day issues and has demonstrated that it can handle them in a democratic manner and with great intelligence.

Gunnar Gundersen, M.D.
La Crosse, Wis.

COUNCIL ON MEDICAL SERVICE

A STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 4

THE DOCTORS HOSPITAL PERINATAL MORTALITY PROGRAM, SEATTLE

The function of the Maternal and Child Welfare Committee of the Washington State Medical Association is "to investigate and compile statistics on the maternal and child welfare status throughout the state and to make recommendations in this field to the Washington State Medical Association." For years a maternal mortality subcommittee has made a study and analysis of each maternal death. In 1955 a subcommittee on perinatal mortality was established with the members appointed by and from the parent committee. The members of this subcommittee and of the full committee recognized the desirability of a statewide study of perinatal deaths but decided that a trial study was necessary first.

Such a pilot program was established at the Doctors Hospital, Seattle, and began operation Jan. 1, 1956. Memberships of the hospital perinatal mortality board includes two obstetricians, two pediatricians, one general practitioner, one pathologist, one surgeon, one internist, one anesthesiologist, and the hospital director. The chairman of this board is also the chairman of the above-mentioned perinatal mortality subcommittee.

Scope of Study

In this study perinatal deaths are defined so as to include only hebdomadal deaths (occurring during the first seven days after birth) and fetal deaths (stillbirths) occurring at 20 or more weeks' gestation. These are the only cases presented to the reviewing board. In addition, however, the chairman reviews all other infant deaths at this hospital and deaths at other hospitals of infants born at this one.

Method of Operation

Case-finding.—For each delivery at the Doctors Hospital information on both mother and infant is summarized on a protocol sheet. Space is reserved for additional remarks by attending physicians. These summary sheets are all routed by the record librarian to the chairman of the perinatal study board, who screens them for perinatal deaths (hebdomadal and fetal). At the end of each month the record room furnishes the chairman with a list of all infant deaths and stillbirths, which serves as a double check for complete follow-up of all perinatal deaths.

Collection of Data.—After experimenting with various questionnaire study forms, the committee is now using a five-sheet protocol. The first sheet is given to the attending physician, who supplies the history and prenatal care data. The second and third are filled out by the chairman of the study group from the delivery data summary sheet and from the hospital records, including autopsy findings. If this does not result in adequate data for committee review, the chairman consults personally with attending physicians, consultants, the anesthesiologist, or others.

Processing of Data.—During the first year of this study monthly meetings were found necessary; these took the form of 7 a. m. breakfast conferences. Attendance has usually been 100%. Each case is presented by the chairman; discussion follows. All procedures, obstetric and pediatric, are analyzed. Page 4 of the protocol has a check list of 15 obstetric and 9 pediatric preventable factors. The committee decides which, if any, of these are appropriate to the case being reviewed. Page 5 of the protocol is designed for summarization of each case by the committee according to the following categories: (1) complications and emergencies (how handled?), (2) drugs (what and when?), (3) nurses' notes (complete?), (4) results of treatment (errors, faulty technique, etc.?), (5) management of mother, (6) management of infant, and (7) conclusions.

Follow-up and Use of Findings.—After a full year's study, the data were summarized in a number of ways, including charts and slides for visual-aid presentation. Each of the deaths considered preventable was described separately with the pertinent facts of the history, a chronological account of the labor and of the infant care given, and the committee's analysis of each case. This material has been presented to the staff of the Doctors Hospital, at staff meetings in other Seattle hospitals, at a meeting of the Seattle Gynecological Society, and at other county society meetings.

This is the fourth of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States Subsequent articles will appear in THE JOURNAL from time to time.

Committee members are W. L. Crawford, M.D , Chairman, Rockford, Ill ; R. B. Chrisman Jr., M.D., Coral Gables, Fla , Philip S Barba, M.D., Philadelphia, Harold S. Morgan, M.D., Lincoln, Neb.; Garland D. Murphy, M D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; J. L. Reichert, M.D., Chicago, Donald A. Dukelow, M.D., Consultant, Chicago, Philip F. Williams, M.D., Consultant, Bala Cynwyd, Pa., Edwin J. Holman, Consultant, Chicago, and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

The Maternal and Child Welfare Committee has authorized the perinatal mortality subcommittee to present programs on the perinatal mortality study to medical and hospital groups throughout the state; invitations from such groups are welcomed. In addition, members of the full committee try to promote interest in starting similar studies in their respective areas of the state. The obstetric consultant to the Washington State Department of Health, who is also a member of the state committee, helps to promote plans for additional perinatal studies on his visits throughout the state.

Regular clinical-pathological conferences on selected perinatal deaths were begun at the Doctors Hospital in the fall of 1957. The entire staff is encouraged to attend.

Results

It was deemed essential to have some statistics for comparison as progress continues in this organized effort to eliminate the preventable factors associated with perinatal deaths. The committee therefore checked the hospital records and compiled a 10-year summary of perinatal mortality for the Doctors Hospital (table 1) with the perinatal mortality rate defined as 1,000 times the ratio of the total number of deaths (i. e., the hebdomadal deaths and fetal deaths occurring at 20 or more weeks' gestation) to the total number of births (live births plus these fetal deaths).

TABLE 1.—*Perinatal Mortality at the Doctors Hospital, 1946-1956**

Year	Total Births (Live and Still)	Hebdomadal Deaths	Fetal Deaths	Deaths/1,000 Births
1946	1,230	29	26	44.7
1947	1,750	28	23	29.1
1948	1,652	27	23	30.2
1949	1,852	38	36	39.9
1950	1,939	35	19	27.8
1951	2,112	38	35	34.1
1952	1,990	33	28	30.6
1953	1,862	25	26	27.4
1954	1,731	31	20	29.1
1955	1,984	37	21	29.2
1956†	2,057	33	17	24.2

*Data from Drs. Paul G. Peterson and Walter S. Keifer of the Doctors Hospital perinatal mortality study board.

†First year of study by hospital perinatal committee.

If the high rate of 1946 is disregarded, it is readily apparent that the perinatal mortality rate during the 10-year period from 1947 through 1956 was relatively static. The fetal death rate decreased from 13.1 to 8.2, but the hebdomadal rate was actually the same (16.0) in 1956 as in 1947. Only slight variations characterized the intervening years.

Of the 33 hebdomadal deaths in 1956, 23 were classified by the committee as nonpreventable, 8 as preventable, and 2 as probably preventable (table 2). The major responsibility in the eight preventable deaths was assigned to the attending physician—seven to the physician making the delivery and one to the physician caring for the infant postnatally. Of the 17 fetal deaths (stillbirths), 13 were classified as nonpreventable and 4 as preventable (table 3). The four preventable fetal deaths (due respectively to ruptured uterus, to diabetes in the mother, to unrecognized brow presentation with birth trauma, and to delay in proper treatment of abruptio placentae) were assigned to the responsibility of the attending physician.

TABLE 2.—*Hebdomadal Deaths at the Doctors Hospital, 1956*

	Previable*	Premature†	Mature‡	Total
Nonpreventable	13	7	3	23
Preventable	0	3	5	8
Probably preventable	0	0	2	2
Total	13	10	10	33

*Less than 1,000 Gm.

†1,000 to 2,500 Gm.

‡More than 2,500 Gm.

Tables 2 and 3 provide an example of the findings of this pilot study. Complete analyses were made relative to deaths at various gradations of weight, to the number of cesarean sections, to multiple births, to the extent of prematurity, and to other aspects of preventability and responsibility. The committee's confidence in its analyses is based to a large extent upon the high percentage of autopsies obtained in 1956. Autopsies were obtained for 41 of the 50 perinatal deaths (82%).

Comments and Conclusions

The sponsors of this pilot study at the Doctors Hospital believe the program has supplied the necessary experience to give direction in program planning for the further reduction of perinatal deaths in the state of Washington. They believe that physicians should take the initiative in establishing a perinatal mortality study program in each hospital. To stimulate and assist in this endeavor, they are presenting the results of the Doctors Hospital experience to county medical societies and major hospitals in the state.

The program has shown, in the vast majority of cases, the true cause and the preventable factors present (if any) in the death of each infant or fetus. The members of the hospital perinatal board believe that some deaths could have been prevented and that the perinatal mortality rate for 1956 should have been at least 25% lower. They emphasize the need for careful postmortem examinations in all perinatal deaths as a prerequisite for valid analyses.

TABLE 3.—*Fetal Deaths (Stillbirths) at the Doctors Hospital, 1956*

	Unclassified	Previable	Premature	Mature	Total
Nonpreventable	2	3	3	5	13
Preventable	0	0	1	3	4
Probably preventable	0	0	0	0	0
Total	2	3	4	8	17

Finally, the sponsors of this project believe that this type of careful analytical and statistical study of all perinatal deaths will add greatly to the quality of obstetrics and pediatrics practiced in any hospital.

MEDICAL NEWS

CALIFORNIA

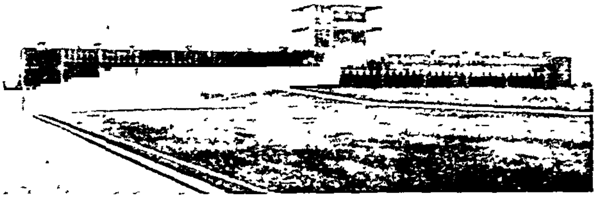
Report of Artery Bank Services.—The anniversary of four years of services by the artery bank at Good Samaritan Hospital in Los Angeles, maintained by the Los Angeles Heart Association, was observed recently. As of June 23, the bank had distributed 925 segments to physicians, mostly for surgery in hospitals in Los Angeles County, according to Dr. Leon J. Tragerman, chairman of the association's Artery Bank Committee. Arteries have been issued for emergency surgery in Arizona, New Mexico, Nevada, and other areas of California. New equipment, recently installed, has reduced the association's cost of processing to $35 a segment. The arteries are provided without charge to the patients, however, as a community service of the heart association. Each segment is inspected, sealed in a tube, labeled, and stored until needed; 1,392 arteries, which are obtained through wills or donations by next-of-kin, have been processed by the artery bank.

CONNECTICUT

Appoint Chairman of Radiology Department.—Dr. Morton M. Kligerman, associate professor of radiology at Columbia University, New York City, has been appointed professor of radiology and chairman of the department of radiology, Yale University School of Medicine, New Haven. Dr. Kligerman will also be radiologist-in-chief at the Grace–New Haven Community Hospital. The hospital and the School of Medicine, affiliated since 1826, form the Yale–New Haven Medical Center. Radiology was established as a full university department this past year and Dr. Kligerman will be the first chairman of the. department. This fall the new Hunter Radiation Therapy Center, under construction, will be opened. Dr. Kligerman served as an officer in the the U. S. Army Medical Corps from 1944 to 1947, and in 1946 became a diplomate of the American Board of Radiology.

ILLINOIS

Illinois Opens Twelfth Mental Hospital.—On Jan. 2 the 14-million-dollar Tinley Park State Hospital was opened. The new unit is located on 412 acres of land southwest of the village of Tinley Park. Presently the two patient facilities with a total bed capacity of 480 consist of a 180-bed acute hospital and a 300-bed semi-infirmary. Administrative offices and central dietary facilities are located in the acute hospital building. Other facilities include a power plant, water treatment plant, sewage treatment plant, incinerator, laundry, and a railroad siding. The hospital is planned for an ultimate expansion to a capacity of 3,500 patients. Funds for the hospital were appropriated by the 65th General Assembly in 1947.



Tinley Park State Hospital.

Chicago

Hospital Alumni Directory.—The Cook County Hospital Internes and Residents Alumni Association has announced that its new directory is being prepared. Members of the association are asked to send their new addresses, if any, to Dr. George C. Blaha, ℅ Cook County Hospital, Chicago. The directory will be available as soon as it has been completed.

Appoint Director for Hospital Planning.—The Hospital Planning Council for Metropolitan Chicago has announced the appointment of Dr. Vane M. Hoge, assistant surgeon general of the U. S. Public Health Service, as its executive director. Dr. Hoge will take over his new position Sept. 15. Among his duties will be continuing research designed to provide an equitable distribution of hospitals, their service requirements, and needs in the metropolitan area. Dr. Hoge is a visiting lecturer on hospital administration at four universities, including Northwestern and the University of Chicago.

Institute for Rehabilitation.—On June 1 the Rehabilitation Institute of Chicago was formally opened as a hospital to admit patients for comprehensive rehabilitation care. For the past three years this institute has been operating as an outpatient clinic. To extend services to bedridden and homebound patients, the board of directors raised funds through individuals and corporations to improve

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

the present facilities, increase the treatment areas, and provide additional accommodations for 75 in-patients. This work has now been completed. A Medical Advisory Committee appointed upon the recommendation of the Chicago Medical Society has formulated the policies under which this institute will operate. Patients with disability arising from disease or accident, except mental, blind or deaf patients, are acceptable for evaluation upon referral from the treating physician or the medical authority representing a recognized health agency. All evaluation and progress reports are sent to the referring doctor. In addition to a comprehensive program in physical rehabilitation, there is a special clinic for cardiac evaluation in relation to work capacity and an amputee clinic for the fitting of prostheses and training in their use. Dr. Edward C. Holmblad is chairman of the Medical Advisory Committee, and Dr. Paul B. Magnuson is founder and honorary chairman of the board of directors. For information write the Rehabilitation Institute of Chicago, 401 E. Ohio St., Chicago 11.

KENTUCKY

Cleft Palate Program.—The Rotary Clubs of Western Kentucky, in conjunction with the Kentucky Crippled Children's Commission, began a program in July, 1957, for aid to persons unable to pay for the repair of cleft palate and hare lip deformities. A team, set up to examine the patient as a group and decide on therapy, consists of a medical man, a plastic surgeon, an E. N. T. man, a prosthodontist, a pedidontist, an orthodontist, a speech therapist, a psychologist, and a nurse. As the program progresses it is planned to extend consultation service to physicians if desired, for patients with these deformities who can afford to pay for these services. Whenever possible the recommended treatments are to be carried on in the home communities, but when such services are not available services of the group can be utilized. No patient can be accepted unless certified by a physician or the local county department of health. The clinic group meets on the first Tuesday of each month at the out-patient department of the Kosair Hospital in Louisville. For information write the Director of the Clinic, % Kentucky Crippled Children's Commission, 1405 E. Burnett Ave., Louisville 17, Ky.

LOUISIANA

Anthrax in Animals.—The U. S. Public Health Service in its Morbidity and Mortality Weekly Report of June 27, states that information has been received from the U. S. Department of Agriculture regarding an increase in incidence of anthrax in northeastern Louisiana. In one parish there have been sporadic cases but this has not been considered an endemic area. It is estimated that more than 250 losses have occurred in cattle, horses, and swine in one parish and 80 losses in another. In two other parishes, five or more cases have been found on different farms. In another parish, which is considered an endemic area, new cases are occurring. These areas are under quarantine, and intensive studies of the disease are under way. One case of human anthrax was reported by the state for the week.

Society News.—The 22d annual meeting of The New Orleans Graduate Medical Assembly will be held March 2-5, 1959, with headquarters at the Roosevelt Hotel. The following officers have been elected for this year: Dr. Joseph O. Weilbaecher Jr., president; Dr. Ambrose H. Storch, president-elect; Dr. Vernon M. Henington, first vice-president; Dr. Willoughby E. Kittredge, second vice-president; Dr. Ralph M. Hartwell, third vice-president; Dr. Maurice E. St. Martin, secretary; and Dr. Boni J. DeLaureal, treasurer.——The Radiological Society of Louisiana has installed the following officers: president, Dr. Joseph T. Brierre, New Orleans; vice-president, Dr. Jerome J. Romagosa, Lafayette; and secretary-treasurer, Dr. Seymour F. Ochsner, New Orleans.

MASSACHUSETTS

Epidemiology Department Head Appointed.—Dr. Brian MacMahon, professor of environmental medicine and community health in the College of Medicine of the State University of New York in Brooklyn, has been named professor and head of the department of epidemiology at the Harvard School of Public Health, Boston, effective Aug. 1. Dr. MacMahon will succeed Dr. John Everett Gordon who retired July 1 to become professor of preventive medicine and epidemiology, emeritus. Dr. MacMahon is a native of Sheffield, England, and received degrees from the University of Birmingham, England, among them the Ph.D. in 1949 and the M.D. (with honors) in 1955. He received the master of science in hygiene from the Harvard School of Public Health in 1953. While at Harvard he was a Rockefeller Foundation fellow in the department of epidemiology, School of Public Health. Prior to coming to the United States in 1955, Dr. MacMahon had served as a lecturer in social medicine at the University of Birmingham. From 1946 to 1948 he was a ship's surgeon in the British Merchant Navy.

MINNESOTA

Workshop on School Health.—The seventh annual School Health and Safety Workshop, sponsored by the Minnesota Department of Education, the Minnesota Department of Health, and the Minnesota Tuberculosis and Health Association, will be held at Camp Lake Hubert near Brainerd, Aug. 17-22. The 1958 workshop is designed for secondary school faculty members who are responsible for health and safety programs. Attendance is limited to recipients of scholarships made available to local teachers by county tuberculosis and health associations as part of the Christmas Seal health education program. Out-of-state staff members will include Fred V. Hein, Ph.D., Chicago, health and fitness consultant, American Medical Association, and Charlotte Leach, New York City, health education consultant, National Tuberculosis Association. Speakers will cover health services, health instruction, healthful school living, safety, nutrition, and dental health. Inquiries may be addressed to Mr. J. G. Neal, Minnesota Tuberculosis and Health Association, 614 Portland Ave., St. Paul, workshop director.

MISSISSIPPI

Establish Department of Anesthesiology.—The department of anesthesiology at the University of Mississippi School of Medicine, Jackson, has been designated a separate department and Dr. Leonard W. Fabian named as professor and chairman. He replaces the late Dr. Glace E. Bittenbender, first professor of anesthesiology at the University of Mississippi Medical Center. Dr. Fabian comes to Mississippi from Duke University School of Medicine, Durham, N. C., where he has been an assistant professor since 1955. He is a diplomate of the American Board of Anesthesiology, member of the American Society of Anesthesiologists and the International Anesthesia Research Society.

State Medical Election.—The Mississippi State Medical Association officers for 1958-1959 are as follows: president, Dr. Guy T. Vise, Meridian; president-elect, Dr. Stanley A. Hill, Corinth; secretary-treasurer, Dr. William E. Lotterhos, Jackson; executive secretary, Mr. Rowland B. Kennedy, Jackson; vice-presidents, Drs. Ashford H. Little, Oxford, Frank C. Massengill, Brookhaven, George G. Townsend, Forest; historian, Dr. David S. Pankratz, Jackson; editor, Dr. William H. Anderson, Booneville; associate editors, Drs. William M. Dabney, Crystal Springs, Louis F. Rittelmeyer, Jackson; speaker of the house of delegates, Dr. Lawrence W. Long, Jackson; vice-speaker of the house of delegates, Dr. Brafton B. O'Mara, Biloxi.

NEW YORK

Neuropsychiatric Research Award.—Dr. Maximilian Fink, director, department of experimental psychiatry, Hillside Hospital, Glen Oaks (Queens), received the first A. E. Bennett Neuropsychiatric Research Foundation award of the Society of Biological Psychiatry May 11. Dr. Fink is secretary of the section of convulsive disorders and brain function of the American Psychiatric Association and president-elect of the Nassau Neuropsychiatric Society. Hillside Hospital, an affiliate of the Federation of Jewish Philanthropies of New York, is a nonprofit, nonsectarian hospital for psychiatric treatment, training, and research. The Hillside research studies have been supported by the National Institute of Mental Health and the board of directors' research fund of the hospital.

Summer Fellowships for Students.—Fellowships have been awarded to 73 students at the State University College of Medicine in Syracuse for research projects this summer at or affiliated with the college. The students will work under supervision of faculty members and will be engaged in research in nearly all departments of the medical college. One student will have a fellowship at the University of California at Los Angeles School of Medicine; a Stanford University School of Medicine student will have a fellowship in the department of psychiatry at the Syracuse College of Medicine; three students who received American Cancer Society fellowships will be assigned to the Memorial Center in New York City to work in the Tumor Clinic there. All fellowships extend over a 10-12 week period. Most students will receive grants of $600 each, with the entire program totaling $43,300. The organizations which have supplied grants for the fellowships are: U. S. Public Health Service, 11 grants; Research Foundation of State University of New York, 7 grants; National Science Foundation, 6 research stipends; Polio Foundation, 8 grants; New York State Health Department, 3 grants; Heart Association of Onondaga County, 4 grants; National Institute of Mental Health, 5 grants; Life Insurance Medical Research Fund, 2 grants.

New York City

City Plans Health Show.—Dr. Leona Baumgartner, New York City health commissioner, has invited national, state, and city officials and voluntary health agencies to take part in a health show, sponsored by the City Health Department, to be held at the New York Coliseum Aug. 6-23 as a health education project of the department. Drug manufacturers also are to be included among the exhibitors. The purpose of the exposition is to show the public what these agencies are doing and are capable of doing to protect and improve public health and what the individual can do to cooperate. Planning for the show is being handled by an advisory committee headed by Mr. Morey R. Fields, chief of the department's Health Education Division.

Heart Research Awards.—Fifty-seven basic and applied research projects in New York City have been approved for financial support by the New York Heart Association for the fiscal year ending June, 1959. For these grants the sum of $368,575 has been allotted. All of these projects fall into one of three general categories, detection, prevention, and cure of heart diseases, and the following subdivisions: surgical diagnosis and treatment, medical diagnosis and treatment, electrocardiography, atherosclerosis, rheumatic fever and rheumatic heart disease, basic research, cardiopulmonary diagnosis, and congenital heart disease. Three types of research awards are made by the association: senior research fellowships, research fellowships, and the "grant-in-aid."

OKLAHOMA

State Medical Election.—Dr. Eldon C. Mohler, Ponca City, assumed the office of president of the Oklahoma State Medical Association May 6. Other officers include: Dr. Alfred T. Baker, Durant, president-elect; Dr. Francis R. First Jr., Checotah, vice-president; Dr. Wilkie D. Hoover, Tulsa, reelected delegate to the A. M. A., and Dr. Joseph L. Duer, Woodward, named alternate; Drs. Clinton Gallaher, Shawnee, and J. Hoyle Carlock, Ardmore, reelected speaker and vice-speaker of the House of Delegates, respectively.

New Hospital in Tulsa.—Groundbreaking ceremonies of the new 8-million-dollar St. Francis Hospital of Tulsa were held April 14. The first main unit will be of 295 beds, with adjoining chapel. Construction on this phase of the project is expected to be completed in the fall of 1959. Long-range plans include a second unit of 295 beds, a convent, chaplain's quarters, and a medical research foundation. The hospital is being built by the William K. Warren Foundation, of Tulsa, a nonprofit institute created by gifts from Mr. William K. Warren, Tulsa oil executive and philanthropist, and Mrs. Warren. The hospital will be operated by a Roman Catholic Order, the Adorers of the Most Precious Blood, of Wichita, Kan.

PENNSYLVANIA

Program to Aid Premedical Education.—The staff of the Medical Clinic of Greenville has announced that it is working with Thiel College to promote interest in premedical education. Thiel College, a coeducational, Lutheran Liberal Arts College in Greenville, in its 93rd year, with an enrollment of 725 students offers cooperative courses in physical therapy, medical technology, nursing, and a premedical course. A special program of independent study and orientation to medical sciences is directed in cooperation with a committee of Greenville physicians. The facilities of the clinic and the Greenville hospital are utilized. To assist in this program, the staff of the clinic has inaugurated a scholarship of $300 a year to premedical students in the junior and senior years. In addition, the college and the clinic are jointly sponsoring a Dr. Joseph A. Doyle Memorial Lecture. Dr. Doyle was one of the founders of the clinic, was an alumnus of Thiel College, and devoted much of his time and effort to both institutions throughout his career as a physician in Greenville. He died shortly after the clinic was founded. The lecture will be delivered this year by Benjamin Tullar, Ph.D., director of research, Sterling-Winthrop Drug Company, to Beta Beta Beta Science Fraternity.

Philadelphia

Phipps Institute to Construct New Plant.—The Henry Phipps Institute for the Study, Treatment, and Prevention of Tuberculosis, of the University of Pennsylvania, is arranging to move from its present location in downtown Philadelphia to a new building to be constructed in West Philadelphia Health Center. Proceeds from the sale of the present site and a recent gift to the University of $53,500 from the family of the late Henry Phipps will be used to construct the new facilities. A portion of the institute's new research laboratories will be built through a U. S. Public Health Service grant of $400,000. The institute will undertake field studies of disease among large population groups. Tuberculosis studies will be continued, but emphasis will be placed on chronic diseases.

Personal.—Dr. Lewis C. Scheffey, of the class of 1915, has received the annual award of the Alumni Association of the Philadelphia College of Pharmacy and Science. Dr. Scheffey, also a graduate of Jefferson Medical College, is president of the Philadelphia Section of the American Cancer Society, president of the American Gynecological Society, and emeritus professor of obstetrics and gynecology at Jefferson.——Dr. Frederick Urbach has been appointed assistant medical director of the Skin and Cancer Hospital of Philadelphia and associate professor of dermatology at Temple University Medical Center, with which the hospital is affiliated.——Dr. John McK. Mitchell, dean of the School of Medicine at the University of Pennsylvania, received an honorary doctor of science degree and was the speaker at Albany Medical College's 1958 commencement exercises May 29.——Dr. Lewis C. Scheffey, emeritus professor of obstetrics and gynecology, Jefferson Medical College and Hospital, received the 35th annual Strittmatter award of the Philadelphia County Medical Society May 14 "in recognition of his devoted service to the welfare of the citizens of Philadelphia and his many contributions to the advancement of medical knowledge."

Name Five 'Pennsylvania Plan' Scientists.—Dr. Norman H. Topping, vice-president for medical affairs at the University of Pennsylvania introduced the first five scholars of the University's Pennsylvania Plan to Develop Scientists in Medical Research to members of the plan's board of directors recently. The five are: Mr. Joseph Sol Eisenman, of Brooklyn, graduate physiology student; Dr. William K. Riker, formerly of New York City, associate in pharmacology; Mr. James W. West, formerly of Cleveland, graduate pharmacology student; Mr. Charles R. Jerge, of East Aurora, N. Y., senior in the school of Dentistry; and Paul T. Cardeilhac, D.V.M., of Washington, D. C., where he was associated with the Walter Reed Army Institute of Research. The Pennsylvania Plan, inaugurated in January of this year, was organized "to accelerate medical progress by alleviating the shortage of researchers and teachers in the basic medical sciences." Under the plan funds up to $7,500 per year will be made available to help "outstanding young medical, dental and veterinary graduates" during a three-year training period for research and training. Dr. Topping announced that the plan hopes to name 15 more scholars by the end of this year.

Revise Postgraduate Program.—The Graduate School of Medicine at the University of Pennsylvania held its first certificate presentation ceremony in its 39-year history May 16 and announced that in the future such exercises will be planned differently due to a major revision in the school's educational program going into effect in the fall. Doctors from all parts of the United States and 16 foreign countries received certificates signifying the completion of an eight-month course in medical specialties and fulfillment of postgraduate requirements in the basic medical sciences. The new, two-semester academic program will be in effect in September. The first four-month period will be called the basic semester, and will consist of a concentrated review in the basic medical sciences with integrated clinical instruction as it applies to the individual specialties. The second, or clinical semester, will be devoted to the clinical (hospital) and applied aspects of these sciences in the particular specialty of the physician-student. According to Dr. George B. Koelle, dean of the Graduate School of Medicine, the revised program will provide an opportunity for doctors just graduating from medical schools to obtain an academic foundation in the specialty of their choice and will be of particular value to foreign physicians and those American doctors who decide to enter specialty training after a period of general practice.

RHODE ISLAND

State Medical Election.—Dr. Francis B. Sargent, Providence otolaryngologist, was installed on May 14 as the 99th president of the Rhode Island Medical Society. Other officers include: vice-president, Dr. Samuel Adelson, Newport; president-elect, Dr. Alfred L. Potter, Providence; treasurer, Dr. Francis V. Garside, Providence; and secretary, Dr. Thomas Perry Jr., Providence.

SOUTH DAKOTA

Summer Research Fellowships for Students.—Twenty-one medical students and two high school juniors are participating in the summer research fellowship program at the University of South Dakota School of Medicine, Vermillion. Under the program, medical students receive a stipend of $200 monthly and are able to pursue individual research projects during the summer months. They are given laboratory space and are assigned to a faculty adviser. The summer program was founded in 1956 by W. L. Hard, Ph.D., dean of the medical school, and chairmen of the medical school departments. The program followed suggestions of medical educators that the medical school curriculum did not allow the student enough time to pursue problems relative to his own interest. Any freshman or sophomore medical student from the university may participate as long as the research facilities do not become overcrowded. Two Mitchell high school juniors interested in science as a career are also assisting in this summer's research program. Several agencies are contributing funds used for paying the monthly stipends, including the American Medical Education Foundation, U. S. Public Health Service, National Foundation for Infantile Paralysis, Lederle Laboratories, Tobacco Industry Research Committee, and the American Medical Association, Council of Foods and Nutrition.

TENNESSEE

Organize Obstetrical Society.—The first meeting of the Tennessee State Obstetrical and Gynecological Society was held April 21 in conjunction with the Tennessee State Medical Association meeting. The society consists of 126 specialists throughout the state. The following officers were elected: Dr. Finis A. Taylor, Memphis, president; Dr. George A. Mitchell, Chattanooga, vice-president; Dr. William F. Mackey, Memphis, executive secretary; and Dr. Homer M. Pace Jr., Nashville, treasurer. Regional secretaries for the four state districts were appointed by their local societies: Dr. James W. Ellis, of Nashville, Dr. Perry J. Williamson, of Knoxville, and Dr. Harry E. Jones, of Chattanooga, along with Dr. Mackey. The next meeting of the society will be in Memphis in 1959 in conjunction with the annual meeting of the state association.

TEXAS

Athletic Team Physicians Organize.—The Texas Society of Athletic Team Physicians decided at its organizational meeting April 19 in Houston to request approval to become a related organization to the Texas Medical Association. Its next annual meeting will be held in conjunction with the association's annual session in San Antonio. Officers elected include Dr. Edward T. Smith, Houston, president; Dr. William H. Ledbetter, Wichita Falls, president-elect; Dr. William S. Horn Jr., Fort Worth, vice-president; and Dr. Jack G. Brannon, Houston; secretary-treasurer. Membership dues are $5. Any member of the Texas Medical Association may join the society. Physicians interested in affiliating with the new organization are invited to write the secretary at 2424 Locke Lane, Houston.

GENERAL

Meeting on Biological Photography.—The 28th annual meeting of the Biological Photographic Association will be held Aug. 18-21 at the Shoreham

Hotel, Washington, D. C. An all-day session will be held at the Walter Reed Army Institute of Research, where members will see the techniques employed by the medical audio-visual department. The four-day program will include presentation of scientific papers; discussion of new techniques and devices, improved methods, and unusual equipment; tours of photographic laboratories; and teaching workshops. The "scientific salon" will feature display of transparencies, prints, and motion pictures. For information write Capt. Stephen P. Dittmann, Medical Audio Visual Department, Walter Reed Army Institute of Research, Washington 12, D. C.

Society News.—Dr. William Malamud, chairman, department of psychiatry, Boston University School of Medicine, is the new president-elect of the **American Psychiatric Association.** Other officers include: vice-presidents, Dr. William B. Terhune, New Canaan, Conn., and Dr. David C. Wilson, Charlottesville, Va., secretary, Dr. C. H. Hardin Branch, Salt Lake City; and treasurer, Dr. Robert H. Felix, Bethesda, Md.——Elected to office at the 47th annual meeting of the **International Academy of Pathology** were: president, Dr. Chapman H. Binford, Washington, D. C.; president-elect, Dr. Robert E Stowell, Kansas City, Kan., and vice-president, Dr. Frederick W. Wiglesworth, Montreal, Canada Dr F. K. Mostofi, Washington, D. C., was reelected to a three-year term as secretary-treasurer. Three new members were elected to the executive council: Dr. George J. Cunningham, London, England, Dr. Benjamin H. Landing, Cincinnati; and Dr. J Lowell Orbison, Rochester, N. Y. Dr. Thomas D Kinney, Cleveland, was reappointed to a three-year term as editor of the academy publication "Laboratory Investigation."——Officers elected by the **American Association of Immunologists** are as follows: president, Dr. Joseph E. Smadel, Bethesda, Md., vice-president, William C. Boyd, Ph D., Boston; and secretary-treasurer, Dr. Calderon Howe, New York City.

Seminar in Brazil on Leprosy.—A seminar on leprosy control organized by the Pan American Sanitary Bureau Regional Office of the World Health Organization, 1501 New Hampshire Ave., N.W., Washington 6, D. C., in collaboration with the government of Brazil, was held in Brazil, June 30-July 7. The seminar was expected to evaluate the extent and scope of the problem of leprosy in this hemisphere, to deal with past results of isolation in the control of leprosy and newer control methods, review mass treatment programs and methods of prevention, and develop recommendations on the organization of leprosy control programs and their integration in the general public health services. Dr. Fred L. Soper, director of the Pan American Sanitary Bureau was in attendance, as was Dr. James A. Doull, leprosy expert of the Leonard Wood Memorial, Washington, D. C. Other participants from the United States included Dr Edgar B Johnwick, medical officer in charge of the leprosarium of the U. S. Public Health Service in Carville, La., and Dr. Frederick C. Kluth, director, division of training of the Texas State Department of Health, in Austin, one of the four states in the U S. where leprosy still occurs There were also participants from Argentina, Brazil, British Guiana, Colombia, Cuba, French Guiana, Jamaica, Martinique, Mexico, Paraguay, Peru, Surinam, Trinidad, Uruguay, and Venezuela. The seminar met in Belo Horizonte, State of Minas Gerias, Brazil, and was attended by some 44 public health workers from 16 countries and territories in the Americas.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	June 28, 1958		June 29, 1957
	Paralytic Type	Total Cases	Total
New England States			
Maine			
New Hampshire			
Vermont			
Massachusetts	2	2	
Rhode Island			
Connecticut			2
Middle Atlantic States			
New York	1	2	6
New Jersey	2	3	3
Pennsylvania			1
East North Central States			
Ohio			
Indiana			2
Illinois	1	1	2
Michigan	1	1	3
Wisconsin			1
West North Central States			
Minnesota			
Iowa		2	2
Missouri			1
North Dakota			
South Dakota		1	1
Nebraska			
Kansas			
South Atlantic States			
Delaware			
Maryland			
District of Columbia			
Virginia		2	
West Virginia		1	1
North Carolina		1	1
South Carolina			7
Georgia	1	1	
Florida		3	5
East South Central States			
Kentucky	2	2	
Tennessee		1	11
Alabama		1	3
Mississippi		2	3
West South Central States			
Arkansas			1
Louisiana	2	2	12
Oklahoma		1	6
Texas	10	20	39
Mountain States			
Montana		1	
Idaho			
Wyoming			2
Colorado			
New Mexico	2	2	
Arizona		1	1
Utah			1
Nevada			
Pacific States			
Washington	1	1	
Oregon	1	1	
California	6	8	11
Territories and Possessions			
Alaska			
Hawaii			
Puerto Rico			
Total	37	70	137

FOREIGN

Meeting on Prevention of Blindness in Brussels.—The general assembly of the International Association for the Prevention of Blindness will be held Sept. 9 in Brussels, Belgium, during the International Congress of Ophthalmology. The program includes the following papers and discussants:

Progress in the Protection Against Occupational Eye Injuries, Dr. W. R. Belfort Mattos, Brazil.
New Aids for the Blind, Prof. Paul Jaensch, Germany.
Test for the Evaluation of Visual Capacity in Industrial and Professional Placement, Dr. Albert D. Ruedemann, Detroit.
Late Complications of Traumatic Lesions of the Cornea and Conjunctiva, Dr. Jules Zanen, Belgium.

For information write Dr. J. P. Mailliart, Secretary General, 47 rue de Bellechasse, Paris 7^e, France.

Congress on Nuclear Biology and Medicine.—The third congress of the Italian Society of Nuclear Biology and Medicine will be held in Florence Nov. 3-4, arranged by the Medical Clinic of the University of Florence. Applications for registration should be sent to the conference Bureau, Clinica medica, Centro Radioisotopi, Viale Morgagni, Firenze, before Sept. 15; the conference fee is of 1500 Lit. for the members of the society and of 3000 Lit. for other participants. Titles and short abstracts of papers (about 200 words) should be submitted before Sept. 15 to the Segreteria della Società Italiana di Biologia e Medicina Nucleare, Clinica Medica, Pisa. The papers accepted will be published in the proceedings of the congress, in a special issue of *Minerva Nucleare.* Twenty-four papers will be selected for presentation during the conference. The following topics will be preferred: new techniques, biological and medical research, and diagnostic use of radioisotopes. Papers covering therapy with external sources will not be accepted, to restrict the topics to be discussed. There will be four joint scientific sessions. The congress president is Prof. Pio Bastai; the secretary is Prof. Gabriele Monasterio.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application was June 23. Dates for the 1959 examinations have been set for Feb. 17 and Sept. 22. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

California: *Written Examination.* Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

District of Columbia:* *Reciprocity.* Washington, September 8. *Examination.* Washington, Dec. 8-9. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Montana: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Hampshire: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 17-18. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

North Carolina: *Reciprocity.* Blowing Rock, July 25. Asst. Sec., Mrs. Louise J. McNeill, Professional Bldg., Raleigh.

Puerto Rico: *Examination.* San Juan, Sept. 2. Sec., Mr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Texas:* *Examination and Reciprocity.* Fort Worth, Dec. 4-6. Sec., Dr. M. H. Crabb, 1714 Medical Arts Building, Forth Worth 2.

Wisconsin: *Examination.* Madison, Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

Arkansas: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

Colorado: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

District of Columbia: *Reciprocity.* Washington, September 8. *Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Kansas: *Examination and Reciprocity.* Kansas City, Nov. 24-25. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

Oklahoma: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Texas: *Examination.* Oct. 13-14. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 19 and Milwaukee, Dec. 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

AIR FORCE

Conference on Orientation Difficulties.—With jets and rocket craft flying at fantastic speeds, even the best-trained pilots find it increasingly difficult to tell exactly where they are, with relation to other planes or to the ground. To explore this question, the U. S. Air Force School of Aviation Medicine called a meeting of specialists on problems of perception in high-speed flight. The group conferred on June 24 and 25 at Randolph Air Force Base. From informal discussions of vestibular physiology and spatial disorientation, the school's physicians hope to plan long-range research to alleviate the flyer's orientational difficulties.

The conference was attended by ear and eye specialists, psychologists, and general physiologists. Dr. John R. Lindsay, from the University of Chicago, was chairman; also from the University was Dr. Cesar Fernandez. Others invited were Dr. Walter H. Johnson from the Defence Research Medical Laboratory in Toronto and Dr. W. J. McNally from the Royal Victoria Hospital of McGill University, Montreal; Dr. Rafael Lorente de No, of the Rockefeller Institute for Medical Research, New York City; Dr. James J. Gibson, Cornell University; Dr. Frank Walsh, Johns Hopkins University; and Dr. George R. Wendt, University of Rochester. Representatives from the Air Force Directorate of Flight Safety Research were Brig. Gen. Sam Neeley and Capt. George H. Normand from Norton Air Force Base, California. Drs. Harlow Ades, W. Brant Clark, and J. I. Niven represented the Naval School of Aviation Medicine, Pensacola, Fla. From the Army Medical Research Laboratory, Fort Knox, Ky., were Drs. Robert L. Cramer and Frederick E. Guedry Jr.

ARMY

General Kirk Receives Alumni Award.—The Board of Directors of the Medical Alumni Association of the School of Medicine of the University of Maryland voted Major Gen. Norman T. Kirk, U. S. Army, retired, to receive the 1958 Alumni Award and Gold Key for outstanding contributions to medicine and distinguished service to mankind. General Kirk served in the U. S. Army Medical Corps for more than 35 years. He was a distinguished orthopedic surgeon before serving as surgeon general of the Army during World War II, for which service he was awarded, by the United States, the Distinguished Service Medal and the Legion of Merit. He received many other military decorations by foreign countries.

NAVY

Retirement of Medical Officers.—The following Navy Medical Corps officers were placed on the retired list on June 30, 1958:

Capt. Arra B. Chesser, completing more than 34 years active duty.

Capt. Vernal G. Backman, having reached the statutory retirement age of 62 after more than 17 years active duty.

Capt. Shirley A. Fuhring, 20 years continuous service.

Capt. Joseph W. Kimbrough, more than 32 years active service.

Capt. John R. Phillips, completing 33 years service.

Capt. Farra L. Read, 31 years active naval service.

Capt. Clark W. Virtue, completing more than 31 years active service.

Capt. David O. Zearbaugh, more than 33 years active service.

Capt. Joseph G. Schnebly was placed on the permanent physical disability retired list on June 1, after completing more than 30 years active service.

Psychiatric Screening for Operation Deep Freeze.—Surgeon General Hogan announces that the Bureau of Medicine and Surgery will provide psychiatric screening for the officers and men of the Naval Support Forces, Antarctica, who will spend winter in the Antarctic as part of Operation Deep Freeze IV. Several psychiatrists and clinical psychologists have been ordered to the Naval Construction Battalion Center, Davisville, R. I., where the processing will take place from June 30 through July 3, 1958. In charge of the screening will be Capt. J. E. Nardini, M.C., chief, Neuropsychiatry Service, Naval Hospital, Bethesda, Md.

Returned to Inactive Duty.—The following Navy Medical Corps officers, who have been serving on active duty in a retired status, were released to inactive duty on June 30, 1958:

Capt. Theodore H. Armstrong
Capt. John P. Denneen
Capt. John J. Goller
Commander Frances B. Eveland
Capt. David D. Greene
Capt. Robert E. Henderson
Capt. Everett B. Keck
Capt. John D. Oyler
Capt. Shelton P. Sanford
Capt. William L. A. Wellbrock
Capt. Arthur L. Kelly
Capt. William W. Kirk
Capt. John H. Kork
Capt. Jay F. Miller

VETERANS ADMINISTRATION

Hospital News.—The V. A. Hospital in the Bronx, New York City, announces that its three-year training program in psychiatry now includes an affiliation with Columbia University. Residents will receive concurrent supervised training in child and in female psychiatry during a full nine months' period at the Columbia University Medical Center and the Psychiatric Institute. This portion of the training program is under the supervision of Drs. Lawrence C. Kolb, Irville H. MacKinnon, and Bernard L. Pacella.

PUBLIC HEALTH SERVICE

Organized Home Care Programs.—At the invitation of the Public Health Service, a group of 23 physicians, nurses, social workers, hospital administrators, and public health officials met in Roanoke, Va., June 9-13, to consider organized home care programs in the United States. There was said to be about 50 programs functioning in this country which provide coordinated health services to patients in their own homes. The group urged more widespread development and support of such community programs by federal, state, and local health and welfare agencies; the health and health-related professions; and health insurance agencies.

The kind of program advocated by the group was defined as follows: "Organized Home Care provides coordinated medical and related services to selected patients at home through a formally structured group comprising at least a family physician, a public health nurse, and a social caseworker, assisted by clerical service. To insure satisfactory functioning of such a service, patients must be formally referred, and there must be an initial evaluation, monthly review of records, and a final discharge conference. There must be ready access to inpatient facilities."

The conference was called by the Chronic Disease Program of the Public Health Service following a recommendation of the National Advisory Committee on Chronic Disease and Health of the Aged to the Surgeon General. Dr. Cecil G. Sheps, general director of Beth Israel Hospital in Boston, and Miss Emilie Sargent, executive director of the Visiting Nurse Association in Detroit, both members of the National Advisory Committee, participated in the conference. Representing their organizations were Dr. Jay Brightman, a member of the Committee on Indigent Care, A. M. A.; Dr. William Stadel, Chairman of the Committee on Chronic Illness, A. M. A.; and Dr. Bernard Bucove, Association of State and Territorial Health Officers. It was agreed that action leading to new and expanded programs should be stimulated by these and other health and social welfare organizations. Publication of the conference proceedings is planned for this fall.

Tuberculosis Detecting Among Students.—The Public Health Service, the Office of Education and Children's Bureau, all in the Department of Health, Education, and Welfare, have recommended that state and local authorities consider replacing compulsory x-ray programs with the tuberculin skin test as the initial means of detecting tuberculosis among students and school employees where experience has shown a low incidence of cases. Their Joint Committee on Health of the School Age Child has urged health authorities to seek changes in laws and regulations which make periodic chest x-ray examinations compulsory, thus paving the way for application of new knowledge and techniques.

Tuberculosis case-finding is an important factor in school and college health programs, the committee pointed out. In the light of changing conditions, however, the value of mass x-ray programs should be weighed against costs and radiation exposure. The Committee also recommended that where x-ray programs are conducted, the equipment be inspected at regular intervals and adequate safeguards used to protect all persons from unnecessary radiation.

New Indian Hospital in New Mexico.—Award of a contract for the construction of a 75-bed Indian hospital, at Shiprock, N. Mex., has been announced by the surgeon general. The Shiprock facility is the first of four new hospitals planned to provide better medical care for Indians and Alaskan natives. The other three will be at Gallup, N. Mex.; Sells, Ariz.; and Kotzebue, Alaska. The general medical-surgical facility will serve about 14,000 of the 82,000 Indians on the Navajo reservation on which the Public Health Service operates a total of five hospitals and maintains contracts with 18 nonfederal hospitals to provide additional services for the Navajos.

The hospital at Shiprock will be a glass-and-brick fireproof structure, partially air-conditioned. It will replace an obsolete building inadequate for modern medical care and will include a contagious disease wing, a complete outpatient department, and a field public health unit.

Directory of U. S. S. R. Medical Institutes.—A revised "Directory of Medical and Biological Research Institutes of the U. S. S. R." has been issued by the National Institutes of Health, Public Health Service. The new edition lists more than 700 institutes with their subdivisions and includes a general subject and name index. Its purpose is to facilitate the exchange of scientific information between the United States and the U. S. S. R., to provide materials for study of the organization of Russian biomedical research, and to assist scientists in planning visits to Russian research centers. A limited supply of the 1958 edition (PHS Publication no. 587) is available. Requests for single copies should be addressed to the Publications and Reports Section, Scientific Reports Branch, National Institutes of Health, Bethesda 14, Md.

Personal.—The surgeon general has announced the appointment of Dr. William H. Stewart as chief of the Service's Division of Public Health Methods. Dr. Stewart formerly was associate director of the National Heart Institute. He has been a commissioned officer of the Public Health Service since 1951, prior to which he was in private practice in Alexandria, La.

DEATHS

Ames, Alfred Charles ⊕ Mountain Grove, Mo.; Starling Medical College, Columbus, 1889; secretary-treasurer of the South Central Counties Medical Society; died in the Burge Hospital, Springfield, May 19, aged 93, of intestinal obstruction.

Anderson, George Minor ⊕ Cheyenne, Wyo.; Rush Medical College, Chicago, 1903; formerly secretary of the state board of health, state health officer, and secretary of the state board of medical examiners; veteran of World War I; past-president of the Laramie County Medical Society; served on the staff of the Memorial Hospital of Laramie County; died in Veterans Administration Hospital May 20, aged 84, of arteriosclerotic heart disease.

Anderson, Robert Virgil, Springfield, Ohio; Indiana University School of Medicine, Indianapolis, 1926; in 1953 became industrial medical officer at Wright-Patterson Air Force Base; died in the Springfield City Hospital May 17, aged 56.

Auslander, Jacob ⊕ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1922; served on the staffs of the Mount Sinai and Sydenham hospitals; died in the Harkness Pavilion of the Presbyterian Hospital June 3, aged 61.

Auyong, Tim Hung, Endicott, N. Y.; Syracuse University College of Medicine, 1922; veteran of World War I; died in the Binghamton City Hospital May 8, aged 63, of myxedema.

Baldwin, Albert Kilburn ⊕ Long Beach, Calif.; Medical School of Maine, Portland, 1911; member of the Massachusetts Medical Society; also an ordained minister; associated with the Long Beach Community, St. Mary's, and Seaside Hospitals; died May 12, aged 80, of cancer of the liver.

Ballard, Charles Sherre, Detroit; University of Michigan Homeopathic Medical School, Ann Arbor, 1908; died in the Jennings Hospital May 17, aged 79.

Barrett, John Milton ⊕ Greenville, N. C.; University of Pennsylvania School of Medicine, Philadelphia, 1926; on the staff of the Pitt Memorial Hospital; died May 2, aged 58, of acute coronary thrombosis.

Barrett, Thomas Francis ⊕ Lackawanna, N. Y.; born in Lackawanna July 22, 1905; Georgetown University School of Medicine, Washington, D. C., 1936; certified by the National Board of Medical Examiners; specialist certified by the American Board of Internal Medicine; formerly on the faculty of Northwestern University Medical School in Chicago, where he was associated with the Veterans Administration Hospital; veteran of World War II; at one time associated with the Veterans Administration Center in Los Angeles; served on the staffs of the Mercy Hospital in Buffalo and Our Lady of Victory Hospital, where he died May 18, aged 53, of coronary heart disease.

Basham, Francis Claybourne ⊕ Eureka, Kan.; Washington University School of Medicine, St. Louis, 1933; founder of the Basham Hospital; died May 22, aged 48, of coronary thrombosis.

Batzdorf, Erwin Erich ⊕ New York City; Schlesische Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau, Prussia, 1912; fellow of the International College of Surgeons; died in the Presbyterian Hospital Feb. 13, aged 71, of carcinoma of the kidney.

Baxter, James William Jr. ⊕ New Albany, Ind.; University of Louisville (Ky.) School of Medicine, 1929; veteran of World War II; died in May, aged 53.

Benbow, John Thomas ⊕ East Bend, N. C.; North Carolina Medical College, Charlotte, 1910; veteran of World War II; died April 5, aged 76, of heart disease.

Berke, Kalman, New York City; Université de Paris Faculté de Médecine, France, 1936; member of the Medical Society of the State of New York; died in the Montefiore Hospital May 18, aged 49.

Berkman, David Mayo ⊕ Oronoco, Minn.; born in Rochester, May 26, 1886; Rush Medical College, Chicago, 1912; on Nov. 1, 1913, joined the Mayo Clinic, in Rochester, as a consultant in medicine and on May 1, 1919, was appointed head of a section of medicine, a post he retained until 1946, when he became a senior consultant, retiring from active practice there on July 1, 1951; member of the board of governors of the Mayo Clinic from 1933 to 1945 and of the board of members of the Mayo Association from 1935 to 1951; emeritus assistant professor of medicine at the University of Minnesota Graduate School, Minneapolis-Rochester; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the Southern Minnesota Medical Association, Alumni Association of the Mayo Foundation, the Society of the Sigma Xi, the Alpha Kappa Kappa and the Psi Upsilon; served in France during World War I; in 1920 was

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⊕ Indicates Member of the American Medical Association.

awarded the degree of master of science from the University of Minnesota; died in St. Mary's Hospital May 28, aged 71, of cerebral hemorrhage and arteriosclerosis.

Bloch, Leon ⊕ Los Angeles; Rush Medical College, Chicago, 1903; specialist certified by the American Board of Internal Medicine; member of the American Gastro-Enterological Association, Illinois State Medical Society, and the Institute of Medicine of Chicago; for many years practiced in Chicago, where he was associated with the Michael Reese and Cook County hospitals; at one time on the faculty of his alma mater; died May 14, aged 79, of uremia.

Brackett, Arthur Stone ⊕ Riverside, Conn.; Jefferson Medical College of Philadelphia, 1895; past-president of the Hartford County Medical Association; served as a member of the board of education and school physician; formerly practiced in Bristol, where he was medical examiner and was associated with the Bristol Hospital; died in Greenwich (Conn.) Hospital May 13, aged 88, of arteriosclerosis.

Bradfield, John Charles ⊕ Logansport, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1903; on the staffs of the Memorial and St. Joseph hospitals; died May 9, aged 79, of heart disease.

Bragger, James Keenan ⊕ Brookline, Mass.; Harvard Medical School, Boston, 1926; veteran of World War II; died in the Veterans Administration Hospital in Boston May 8, aged 60, of carcinoma of the left lung.

Brault, Norbert Romulus, New Bedford, Mass.; School of Medicine and Surgery of Montreal, Que., Canada, 1913; served on the staff of the Acushnet (Mass.) Hospital, where he died May 15, aged 67.

Brew, Mary Frances ⊕ Syracuse, N. Y.; Cornell University Medical College, New York City, 1920; specialist certified by the American Board of Psychiatry and Neurology; served on the faculty of the State University of New York College of Medicine; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; for many years assistant director of the Syracuse Psychopathic Hospital; formerly associated with the Binghamton (N. Y.) State Hospital; died in University Hospital May 19, aged 66, of a ruptured aortic valve.

Brian, Frederick Willard ⊕ Bloomington, Ill.; Northwestern University Medical School, Chicago, 1911; fellow of the International College of Surgeons; member of the Industrial Medical Association; veteran of World War I; died in the Presbyterian Hospital May 31, aged 74, of myocardial infarction and cancer of the stomach.

Brill, Alton Abraham ⊕ New York City; University and Bellevue Hospital Medical College, New York City, 1910; died May 4, aged 69, of uremia and arteriosclerotic heart disease.

Brock, DeWitt Talmage ⊕ Jackson, Miss.; Atlanta College of Physicians and Surgeons, 1913; veteran of World War I; associated with the Mississippi Baptist Hospital and St. Dominic–Jackson Memorial Hospital; died May 20, aged 68, of cancer of the pancreas.

Brown, Byron J., St. Petersburg, Fla.; University of Vermont College of Medicine, Burlington, 1893; veteran of World War I; for many years practiced in Providence, R. I., where he was on the staff of the Roger Williams General Hospital; died in Bay Pines May 7, aged 87, of lymphosarcoma.

Bryant, Mason David ⊕ Lowell, Mass.; Columbia University College of Physicians and Surgeons, New York City, 1905; for many years medical examiner for Middlesex County; on the staffs of the Lowell General and St. Joseph's hospitals; died May 8, aged 75, as the result of an automobile accident.

Carmichael, Charles S., Fort Atkinson, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1907; died May 1, aged 79.

Cary, Dale Emerson ⊕ Lancaster, Pa.; Jefferson Medical College of Philadelphia, 1911; past-president of the Lancaster City and County Medical Society; served as mayor of Lancaster; formerly medical director of the Rossmere Sanatarium; associated with the Lancaster General Hospital, where he died May 19, aged 77, of a cerebral vascular accident.

Chisholm, George H., Texarkana, Texas (licensed in Texas in 1903); died May 2, aged 91.

Dew, Hogan Allen ⊕ Warren, Ark.; University of Arkansas School of Medicine, Little Rock, 1939; veteran of World War II; died May 7, aged 40.

Dixon, George Grady ⊕ Ayden, N. C.; born in Winterville April 29, 1890; Medical College of Virginia, Richmond, 1915; member of the House of Delegates of the American Medical Association from 1947 to 1949; member of the American Academy of General Practice; a member of the state board of health since 1930 and was serving his third term as its president; veteran of World War I; past-president of the Pitt County Medical Society; member of the county board of health; chairman of the board of trustees and a member of the commission on finance; instrumental in organizing the Ayden Rotary Club and served as its first president; since 1933 president of the First National Bank; associated with the Pitt Memorial Hospital; died near Hickory May 7, aged 68, of a heart attack.

Dodd, Charles Singleton ⊛ Petersburg, Va.; Medical College of Virginia, Richmond, 1904; died May 13, aged 77.

Dollman, C. Mazarin Campbell ⊛ Washington, D. C.; George Washington University School of Medicine, Washington, 1907; served on the faculty of the Georgetown University School of Medicine; veteran of World Wars I and II; for many years on the staff of Garfield Memorial Hospital and medical director of the Washington Home for Incurables; died in the Walter Reed Army Hospital May 13, aged 79, of myocardial infarction and arteriosclerotic heart disease.

Dziuk, Walter Anthony ⊛ Chicago; Chicago Medical School, 1930; served on the faculty of his alma mater; past-president of the Northwest Branch of the Chicago Medical Society; veteran of World War I; died in St. Mary of Nazareth Hospital May 21, aged 60, of acute posterior myocardial infarction.

Epting, Monroe Jacob ⊛ Savannah, Ga.; born in Savannah July 29, 1898; University of Virginia Department of Medicine, Charlottesville, 1923; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; veteran of World War I; during World War II served overseas in the Pacific theater as regimental surgeon with the Third Medical Battalion, Third Division, Fleet Marine Force; was awarded the divisional citation for service at Bougainville and the Bronze Star while serving on the island of Guam; recalled to active duty in the medical corps of the U. S. Naval Reserve, serving until 1951; past-president of the Medical Association of Georgia; associated with the Oglethorpe Sanatorium and Telfair Hospital; died May 8, aged 59.

Eversole, George Edwin, New York City; Harvard Medical School, Boston, 1913; died in the University Hospital April 5, aged 73, of myocardial infarction.

Ferguson, Rutherford Hayes ⊛ Victoria, Texas; Medico-Chirurgical College of Philadelphia, 1906; formerly practiced in Pittsburgh, where he was associated with the Western Pennsylvania and South Side hospitals; died May 1, aged 82, of myocardial failure.

Geary, Riley Lavender ⊛ Ruth, Nevada; State University of Iowa College of Medicine, Iowa City, 1953; veteran of World War II; member of the American Academy of General Practice; on the staff of Steptoe Valley Hospital, East Ely; died in the Lutheran Hospital, Los Angeles, May 2, aged 32, of pneumonitis and embryonal carcinoma of the testicle.

Gilliatt, James Price ⊛ Salem, Ind.; University of Louisville (Ky.) School of Medicine, 1941; veteran of World War II; county health officer; on the staff of the Washington County Memorial Hospital; died May 7, aged 57, of cancer of the lung.

Glas, Emil, New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1901; specialist certified by the American Board of Otolaryngology; an associate member of the American Medical Association; died in the Lenox Hill Hospital May 19, aged 79.

Gray, Frederick James Jr. ⊛ Little Rock, Ark.; born in Knoxville, Tenn., Sept. 28, 1919; Vanderbilt University School of Medicine, Nashville, Tenn., 1943; assistant clinical professor of surgery at the University of Arkansas School of Medicine; specialist certified by the American Board of Surgery and the American Board of Thoracic Surgery; member of the American Trudeau Society and past-president of the Arkansas Chapter; fellow of the American College of Surgeons; veteran of World War II; associated with Arkansas Baptist, Arkansas Children's, and Veterans Administration hospitals and St. Vincent Infirmary; died in Hot Springs May 7, aged 38.

Griffin, Claude ⊛ Atlanta, Ga.; Atlanta College of Physicians and Surgeons, 1911; veteran of World War I; past-president of the Georgia State Board of Medical Examiners; served on the staffs of the Georgia Baptist and Piedmont hospitals; died May 8, aged 69, of a heart attack.

Gulezian, Lucy E. H., Philadelphia; Temple University School of Medicine, Philadelphia, 1914; formerly resident physician at the Woman's Hospital and on the staff of the Hospital of the University of Pennsylvania, where she died May 12, aged 79.

Hancock, Meda Walton, Dora, Ala.; University of the South Medical Department, Sewanee, Tenn., 1908; died in Woodward March 15, aged 74, of arteriosclerosis and cerebral hemorrhage.

Hancock, William Scott Jr., Brooksville, Fla.; Atlanta School of Medicine, 1913; died in the G. Pierce Wood Memorial Hospital, Arcadia, March 21, aged 74, of arteriosclerotic heart disease.

Hatch, Philip Luther, Union City, Pa.; Cleveland Medical College, Homeopathic, 1897; served overseas during World War I; died May 1, aged 86.

Herman, Boris Solomon ⊛ San Francisco; College of Physicians and Surgeons of San Francisco, 1919; died May 7, aged 67, of coronary thrombosis.

Herman, Maxwell ⊛ Philadelphia; Jefferson Medical College of Philadelphia, 1909; specialist certified by the American Board of Ophthalmology; at one time associated with the Indian Service; emeritus chief of ophthalmology at Albert Einstein Medical Center; died May 16, aged 69, of acute coronary occlusion.

Hertz, William J. ⊕ Allentown, Pa.; Medico-Chirurgical College of Philadelphia, 1898; specialist certified by the American Board of Otolaryngology; past-president of the Lehigh County Medical Society and the Reading (Pa.) Eye, Ear, Nose, and Throat Society; fellow of the American College of Surgeons; associated with Allentown Hospital and the Sacred Heart Hospital, where he died May 4, aged 81, of coronary occlusion.

Hill, Aymer Seth Columbus ⊕ Winooski, Vt.; University of Vermont College of Medicine, Burlington, 1898; formerly assistant professor of clinical medicine at his alma mater; associated with the Fanny Allen, Mary Fletcher, and De Goesbriand hospitals; died May 8, aged 81, of abdominal malignancy.

Horowitz, Meyer, New York City; St. Louis University School of Medicine, 1927; member of the Medical Society of the State of New York; died in the Beekman-Downtown Hospital March 18, aged 59, of arteriosclerotic heart disease.

Jansen, Richard William, Richmond Heights, Mo.; St. Louis College of Physicians and Surgeons, 1918; physician for the board of education; died in St. Louis, April 30, aged 66, of coronary thrombosis.

Jeffery, Leon Abram, Daytona Beach, Fla.; Louisville (Ky.) Medical College, 1907; died April 21, aged 88, of cerebral hemorrhage and hypertension.

Kristeller, Leo, New York City; University and Bellevue Hospital Medical College, New York City, 1912; on the staff of the Gouverneur Hospital; died in the Medical Arts Center Hospital April 22, aged 78, of arteriosclerotic heart disease, chronic bronchitis, and emphysema.

Little, William Arthur Jr., Lieut., U. S. Navy, retired, Liberty, N. Y.; Albany (N. Y.) Medical College, 1942; certified by the National Board of Medical Examiners; interned at the U. S. Naval Hospital in Newport, R. I.; served a residency at the Naval Hospital in Philadelphia, Langley Porter Clinic in San Francisco, River Crest Sanitarium in Long Island City, and the Southside Hospital in Bay Shore; retired from the U. S. Navy April 1, 1950; died March 14, aged 41, of lobar pneumonia.

Logan, Archibald Hodge ⊕ Rochester, Minn.; born in Pittsburgh June 25, 1877; University of Pennsylvania Department of Medicine, Philadelphia, 1907; at one time instructor in medicine at the University of Pittsburgh School of Medicine; became assistant in the division of medicine at the Mayo Clinic in 1910 and the following year was appointed head of a section of medicine, a post he held until becoming senior consultant in 1942; from 1925 through 1929 served as faculty chairman of the Mayo Clinic; retired April 1, 1946; emeritus associate professor of medicine at the University of Minnesota Graduate School, Minneapolis-Rochester; veteran of the Spanish-American War; specialist certified by the American Board of Internal Medicine; received the honorary degree of master of science in 1930 and in 1934 the honorary degree of doctor of science from Washington and Jefferson College in Washington, Pa.; in 1938 president of the Rochester chapter of alumni of the University of Pennsylvania; in 1940 was awarded the silver medal in the scientific exhibit of the American Medical Association for an exhibit on polyps of the rectum and colon; served on the staffs of the Kahler and St. Mary's hospitals; from 1928 to 1953 served as chairman of the board of directors of the Logan-Gregg Hardware Company of Pittsburgh; died in St. Mary's Hospital May 1, aged 80, of ruptured thoracic aneurysm.

Lynch, Delia Adeline, Omaha; John A. Creighton Medical College, Omaha, 1909; died May 3, aged 83, of posterior coronary occlusion.

Meade, John Richard ⊕ St. Paul; University of Minnesota Medical School, Minneapolis, 1930; clinical instructor in medicine at his alma mater; specialist certified by the American Board of Internal Medicine; member of the American Diabetes Association, Minnesota Society of Internal Medicine, Alumni Association of Mayo Foundation and Alpha Kappa Kappa; on the staffs of the Ancker, St. Joseph's, Miller, St. Luke's, and Gillette State hospitals; died May 4, aged 55, of coronary occlusion.

Merkel, Arthur Edwin ⊕ Des Moines, Iowa; University of Nebraska College of Medicine, Omaha, 1905; member of the Industrial Medical Association; past-president of the Polk County Medical Society; during World War I chief of a medical examination board for the draft and served on the medical examination board for selective service during World War II; associated with Broadlawns, Iowa Methodist, Mercy, and Iowa Lutheran hospitals; died May 6, aged 78, of arteriosclerosis.

Moore, William Robert ⊕ Cleveland; Indiana University School of Medicine, Indianapolis, 1952; associated with the Deaconess Hospital; died in Medina May 4, aged 32, in a private airplane crash.

O'Reilly, Patrick J., Detroit; Saginaw (Mich.) Valley Medical College, 1902; died March 22, aged 79, of a cerebral vascular accident, diabetes mellitus, and chronic lymphatic leukemia.

Padula, Vincent Domenica ⊕ Wethersfield, Conn.; Regia Università degli Studi di Roma, Facoltà di Medicina e Chirurgia, Italy, 1935; veteran of World War II; member of the staff of St. Francis Hospital in Hartford, where he died May 10, aged 53, of coronary thrombosis.

Pellini, Emil John, Putnam Valley, N. Y.; born in New York City Dec. 6, 1888; University and Bellevue Hospital Medical College, New York City, 1915; veteran of World War I; fellow of the New York Academy of Medicine; member of the Society for Experimental Biology and Medicine, Harvey Society, and the New York Heart Association; for many years on the faculty of his alma mater; from 1924 to 1929 associate professor of pharmacology at the New York University College of Dentistry; from 1919 to 1927 therapist, cardiac clinic, social service, Bellevue Hospital in New York City; consulting pharmacologist for Merck & Company in New York City from 1924 to 1927; died in Miami, Fla., May 5, aged 69, of cancer of the lung.

Pfaff, Norman Joseph ⊕ Rochester, N. Y.; University of Buffalo School of Medicine, 1917; fellow of the American College of Surgeons; veteran of World War I; on the staffs of the Monroe County Infirmary and St. Mary's Hospital, where he died May 3, aged 63.

Plaut, Carl, New York City; Ludwig–Maximilians–Universität Medizinische Fakultät, München, Bavaria, Germany, 1901; died in the Mount Sinai Hospital April 21, aged 80, of acute myocardial infarction and abdominal carcinoma.

Post, Lawrence Tyler ⊕ St. Louis; born in St. Louis in 1887; Johns Hopkins University School of Medicine, Baltimore, 1913; professor emeritus of ophthalmology, Washington University School of Medicine, where he retired as head of the department in 1953, a post he held for 20 years; specialist certified by the American Board of Ophthalmology; chairman, Section on Ophthalmology of the American Medical Association, 1941-1942; member and past-president of the American Academy of Ophthalmology and Otolaryngology; member and past-president of the American Ophthalmological Society, which in 1947 awarded him the Lucien Howe Medal; past-president of St. Louis Ophthalmic Society; received the Leslie Dana Gold Medal for 1948, given by the National Society for the Prevention of Blindness; served as a member of the National Research Council's Subcommittee on Ophthalmology; fellow of the American College of Surgeons; veteran of World War I; for many years editor of the *American Journal of Ophthalmology*; associated with Washington University Clinics, St. Louis Maternity and St. Louis Children's hospitals, and the Barnes Hospital, where he died May 13, aged 70, of bronchopneumonia.

Rea, Greene Lee ⊕ Charlotte, N. C.; North Carolina Medical College, Davidson, 1906; service member of the American Medical Association; served as city health officer; formerly associated with the Veterans Administration retiring Jan. 31, 1957; died in the Presbyterian Hospital May 5, aged 78.

Rees, David Llewelyn ⊕ Pittsburgh; Western Reserve University School of Medicine, Cleveland, 1917; member of the staff of the Passavant Hospital in Pittsburgh; died May 8, aged 65, of myocardial infarction.

Reger, Earl Lee ⊕ Spokane, Wash.; College of Physicians and Surgeons, Baltimore, 1907; veteran of World War I; on the staffs of the Sacred Heart and Deaconess hospitals; died April 3, aged 82, of arteriosclerosis.

Ringa, John Peter ⊕ Chicago; Chicago Medical School, 1934; on the staffs of the Martha Washington and Walther Memorial hospitals; died May 15, aged 54, of myocardial infarction.

Roan, Avery Mabry ⊕ Decatur, Ala.; Chicago College of Medicine and Surgery, 1914; member of the American Academy of General Practice; on the staff of the Decatur General Hospital; died in the Lisenby Hospital, Panama City, May 2, aged 71, of coronary thrombosis and cerebral vascular accident.

Rockman, Jacob, Miami Beach, Fla.; Cornell University Medical College, New York City, 1911; specialist certified by the American Board of Pathology; died in the Mount Sinai Hospital March 19, aged 72.

Rytel, Pauline Josephine ⊕ Chicago; Uniwersytet Jozefa Pilsudskiego, Warszawa, Poland, 1927; interned at the Norwegian American Hospital; died in the Albert Merritt Billings Hospital May 5, aged 55, of uremia, nephrosclerosis, and hypertension.

Saffier, Isidor Jacob, Brooklyn; Eclectic Medical College of the City of New York, 1910; died April 29, aged 75, of coronary sclerosis.

Sagi, Eugene S., Jackson Heights, N. Y.; Magyar Kiralyi Pazmany Petrus Tudomanyegyetem Orvosi Fakultasa, Budapest, Hungary, 1914; director of the Sagi Cancer Research Center at University Hospital (New York University–Bellevue Medical Center); died May 15, aged 66.

Schaff, George K., Plymouth, Ind.; Chicago College of Medicine and Surgery, 1913; died in Victoria, Texas, April 25, aged 88.

Schrage, Benjamin Leon, New York City; Eclectic Medical College, Cincinnati, 1923; member of the Medical Society of the State of New York; on the staff of the Manhattan General Hospital; died May 19, aged 61, of coronary occlusion.

Schroeder, George Fred C. ⊕ Itasca, Ill.; Northwestern University Medical School, Chicago, 1905; served as an Itasca village trustee and president; associated with the Memorial Hospital of DuPage County in Elmhurst; died in Villa Park May 18, aged 80.

Sitchevska, Olga Lazarovna ⊕ New York City; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1918; specialist certified by the American Board of Ophthalmology; fellow of the American Academy of Ophthalmology and Otolaryngology and the New York Academy of Medicine; member of the Association for Research in Ophthalmology; on the staffs of the New York Infirmary and New York Eye and Ear Infirmary; died May 20, aged 62, of coronary thrombosis.

Smith, James Stokes ⊕ Miami, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1930; member of the American Academy of General Practice; held the Purple Heart Medal with an Oak Leaf Cluster and the Legion of Merit for service during World War II and was one of the survivors of the Bataan Death March; a retired lieutenant colonel in the Florida National Guard; associated with the North Shore Hospital; died in the Cleveland Clinic Hospital, Cleveland, Ohio, May 17, aged 51, of a cardiovascular accident.

Smith, Lucian Conway, Lake Worth, Fla.; George Washington University School of Medicine, Washington, D. C., 1905; died March 31, aged 82, of arteriosclerotic heart disease.

Smith, Robert Emmett ⊕ Springfield, Ill.; Northwestern University Medical School, Chicago, 1914; served overseas during World War I; associated with St. John's Hospital, where he died May 7, aged 67, of dissecting aneurysm of the abdominal aorta.

Staver, Benjamin Franklin ⊕ Bartlesville, Okla.; University Medical College of Kansas City, Mo., 1904; died in Salt Lake City April 5, aged 79.

Thomas, William Harper ⊕ McGregor, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; veteran of World War I; public health officer for the town of McGregor for many years; died May 7, aged 78.

Trumbull, Robert Augustus ⊕ Dallas, Texas; Southern Methodist University Medical Department, Dallas, 1913; past-president of the Dallas County Medical Society; veteran of World Wars I and II and received the Distinguished Service Medal; died May 12, aged 68, of bronchogenic cancer with cerebral metastases.

Valz, Edward Victor ⊕ Commander, U. S. Navy, retired, Philadelphia; born in Baltimore Dec. 5, 1878; University of Virginia Department of Medicine, Charlottesville, 1903; appointed to the rank of lieutenant (jg) in the Navy Medical Corps on March 5, 1907, and was assigned to duty at the Naval Medical School, Washington, for duty; advancing progressively through the commissioned ranks of the Navy Medical Corps, attained the rank of commander in January, 1925; placed on the retired list of Navy officers on June 30, 1937, after completing more than 30 years naval service; in 1939 recalled to active duty in a retired status and was assigned to the Navy Receiving Station, Philadelphia; served there until his release to inactive duty in November, 1942; during his Naval career, served with the Navy Medical Department throughout the United States and abroad and in ships of the fleet; at the time of his retirement in 1937 was serving on duty at the Marine Recruiting Station, Philadelphia; life member of the Association of Military Surgeons of the United States; died in the U. S. Naval Hospital May 9, aged 79, of a cerebrovascular accident.

Waddington, Joseph E. G. ⊕ Detroit; Indiana College of Medicine and Midwifery, Indianapolis, 1886; died in the Sinai Hospital May 11, aged 93.

Walker, William Clarence ⊕ Salt Lake City; University of Tennessee College of Medicine, Memphis, 1929; member of the American College of Chest Physicians; fellow of the American College of Physicians; past-president of the staff, Holy Cross Hospital; died May 8, aged 56.

Walker, William Joseph ⊕ New York City; Cornell University Medical College, New York City, 1908; fellow of the American College of Physicians; emeritus consultant in medicine, Fordham Hospital and Bronx Eye and Ear Infirmary; for many years surgeon for the New York City Police Department; died in St. John's Riverside Hospital, Yonkers, May 18, aged 74, of uremia.

Waterman, Wayne Riley, Brooklyn; Eclectic Medical College, Cincinnati, 1919; veteran of World War I; died in the Samaritan Hospital April 10, aged 68, of acute myocardial infarction.

Whaley, James Higgins Jr., New York City; Cornell University Medical College, New York City, 1926; veteran of World Wars I and II; died April 24, aged 61, of coronary occlusion, arteriosclerosis, and cerebral arteriosclerosis.

Williams, Daniel Hix, Dallas, Texas (licensed in Texas, under the Act of 1907); died April 24, aged 83.

Wisely, Martin Robert ⊕ Edenton, N. C.; University of Virginia Department of Medicine, Charlottesville, 1935; member of the American Academy of General Practice; veteran of World War II and received the Silver Star Medal; died May 11, aged 46, of a heart attack.

Wright, Preston Elijah, Golden, Colo.; Chicago College of Medicine and Surgery, 1909; formerly practiced in Golconda, Ill., serving as health officer of quadri, consisting of Hardin, Johnson, Massac, and Pope Counties; died April 2, aged 73, of coronary occlusion.

FOREIGN LETTERS

AUSTRIA

Complications of Cortisone Therapy.—At the meeting of the Society of Physicians in Vienna on May 30 Dr. E. Keibl reported on a 27-year-old woman with chronic secondary polyarthritis. Her mitral stenosis was completely compensated. An acquired hemolytic anemia had been present for four years. On admission the erythrocyte count was 1,600,000 per cubic millimeter. Treatment with cortisone resulted in a complete remission. This treatment was discontinued abruptly on account of epileptiform paroxysms. In addition to a hemolytic crisis a severe pancarditis developed on the 12th day after discontinuation of cortisone. Treatment with cortisone was resumed, and the patient improved. A splenectomy was performed, which resulted in a complete hematological remission. This had continued for one year when the patient was last seen.

Hibernation for Cranial Injuries.—At the same meeting Dr. O. Mayerhofer presented two 11-year-old boys who had been admitted with severe injuries of the base of the cranium. They were treated by artificial hibernation, since the foci of the injuries were not accessible. The first child was so treated for 16 days. Consciousness returned around the 32nd day. Treatment resulted in complete clinical cure with slight psychic defects and a definitely abnormal electroencephalogram. The second child was so treated for 30 days. Consciousness returned around the 34th day. All motor disturbances disappeared, but there were residual psychic defects and some electroencephalographic changes. The principle of this treatment is immobilization and prevention of spasms and fever. During this time the primary foci of the injury have time to heal. The problem of nutrition is of great importance. In the beginning food must be given intravenously and later by means of gavage. This treatment requires a great amount of nursing care. Dr. Kucher reported a series of six patients with severe cranial injuries who were treated successfully with artificial hibernation. It seems that the brain of a person in whom hypothermia has been induced is capable of regenerating after an injury that would otherwise have proved fatal.

Complications After Cortisone Therapy.—Dr. G. Geyer at the same meeting stated that when cortisone treatment is discontinued for some time, severe complications such as acute collapse may occur, especially if the patient is exposed to trauma or similar stress. A relative insufficiency of the adrenal gland occurs because cortisone therapy destroys the regulatory influence of the pituitary gland. Acute recurrent rheumatic diseases may be observed after discontinuation of the cortisone therapy. In some instances these recurrences and phases of adrenal insufficiency occurred simultaneously after cortisone therapy. To prevent such recurrences it is necessary to avoid adrenal insufficiency. Thus the discontinuation of treatment with cortisone demands administration of corticotropin.

Prostatic Retention of Urine.—At the March meeting of the Austrian Urological Society Dr. I. Tham reported on a series of 215 patients with severe prostatic retention of urine. On 110 of these a prostatectomy was performed. On 57 electroresection was carried out and only 22 were sent home with an indwelling catheter. The remaining patients were able to urinate spontaneously and had no residual urine. Most of the patients operated on were not in a good condition preoperatively, and many had evidences of renal damage. The average age of the patients subjected to prostatectomy was 70, and of those subjected to electroresection it was 74. Wide indications were applied because this policy is believed to be more beneficial to the patient than extreme conservatism. The death rate for patients subjected to prostatectomy was 6.3%, and for those subjected to electroresection it was 1.3%.

BRAZIL

Tubal Occlusion.—Dr. C. A. Ferreira (*An. brasil. ginec.* 45:133, 1958) reported a series of 865 women with tubal occlusion. The two principal methods of diagnosis were hysterosalpingography accompanied by fluoroscopy and by tubal insufflation. In all patients these examinations were made only after determining the sedimentation rate and treating any inflammatory process present. Of the 336 women who submitted to the necessary tests tubal insufflation alone was used in 160, hysterosalpingography alone in 78, and both methods in 98. These examinations disclosed complete tubal occlusion in 146. Most of them were treated by antibiotics, short wave diathermy, and roentgentherapy until the sedimentation rate became normal or the patient was clinically cured. When uterine or tubal

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The items in these letters are contributed by regular correspondents in the various foreign countries.

hypoplasia was suspected hormonal treatment was given. Repeated tubal insufflations were then performed in order to overcome the occlusion. If this did not reestablish the tubal patency, intratubal injections containing antibiotics, hyaluronidase, and hydrocortisone were given. The latter treatment caused reestablishment of patency in several patients and made subsequent pregnancy possible for a few. If these treatments failed, surgery was suggested; 27 patients were operated on with variable results. Nine patients were subjected to ovariouterine implantation, one of them subsequently undergoing three pregnancies terminated by miscarriage. In seven patients salpingostomy was performed, with patency reestablished for a few months but no pregnancies. In 11 patients reimplantations were performed, with 100% patency in the first four months and two pregnancies. Of these 11 patients, 5 were followed up and showed subsequent occlusion. These were new occlusions, since, with the exception of a case of isthmic relapse, all the patients presented ampullar occlusion or peritubal blocking. These new obstructions, the greatest problem of tubal surgery, appear if the patients do not become pregnant during the first year. They result from new inflammatory outbreaks rather than from poor surgical results.

The prevention of tubal occlusion depends on early discovery of endocrine troubles in adolescence, teaching of sexual hygiene, prevention of venereal diseases, prenuptial instruction and medical examination, and instruction in contraception. In 84 of these patients with tubal occlusion a history of spontaneous or induced miscarriage or the use of intrauterine injections as a contraceptive measure was obtained. This represented an incidence of 62% of tubal occlusion, which greatly exceeded the rate for the 200 patients (31%) without such a history.

Increased Epinephrine Production in Hemorrhagic Shock.—Prof. P. S. Lacaz and co-workers (*Rev. brasil. cir.* 35:3, 1958) found that in dogs subjected to hemorrhage, and thus in a state of arterial hypotension, some hypertensive substance was released that could be recognized in receptor dogs injected with blood from the shocked animals. In the dogs subjected to hemorrhage, as the blood pressure fell, the blood sugar level increased markedly. In a typical dog, as the blood pressure fell from 110 to 20 mm. Hg, the blood sugar level rose from 75 to 367 mg. per 100 ml. These results led to the assumption that the hypotensor effect might be due to epinephrine. With use of yohimbine as an adrenergic blocking drug it was possible to invert the hypertensive effect in the receptor dogs. Repeated in animals with renal and suprarenal veins ligated, the experiments showed the same results. Thus it was concluded that the substance appearing in the blood of donor dogs was epinephrine. No consistent increase of arterenol occurred, since with doses of yohimbine that might invert the effects of epinephrine but were unable to invert those of levarterenol they did not obtain responses of the levarterenol type. The effects on the blood pressure showed that epinephrine was present in larger and larger amounts in the preagonal, agonal, and the postmortem stages of hemorrhagic shock. Ligature of the adrenal veins did not change the effects observed, which in these conditions were due to epinephrine originating outside of the adrenals, for example, in the paraganglia. The paradoxical effects presented above might be due to different mechanisms, to be clarified in subsequent experiments. The authors admitted that a lowering of the enzymatic effects that normally destroy epinephrine is present in shock. If this hypothesis could be proved it would be permissible to admit the desribed phenomenon as an indication of the irreversibility of shock.

CANADA

Hospital Insurance.—Dr. Morley Young (*Canad. M. A. J.* 78:754, 1958) stated that the increased demand for hospital services after introduction of a universal insurance plan may stem from the patient's desire to get his money's worth and from the physician's desire to get the best care for his patient. This approach may not be economically unsound. The admission rate increases with increased availability of beds up to a certain level, when it tapers off to a plateau. Thus a plateau has been reached in Saskatchewan with about 8 beds per 1,000 population, in Alberta, with 7, and in British Columbia with 5.3. The Saskatchewan experience shows that rural areas, towns, and villages have a higher admission rate than metropolitan areas, but the length of stay is greater in city hospitals. Long-term cases account for a high percentage of hospital days; for example, in Alberta persons staying 20 days or more account for 95% of admissions and 72% of hospital days. The number of surgical operations and obstetric cases increases with availability of beds. Dr. Young foresees a time when almost all of a physician's work will be conducted in hospital or office and all physicians will have to have hospital privileges. Although on the whole hospital insurance has been a good thing for both patient and physician, it introduces certain evils, such as the tendency to keep patients in hospital too long, to admit them for investigation which might have been done outside with a little more effort, and to lower treatment standards if staffing is inadequate.

Dr. F. B. Roth stated that since under a universal hospital insurance plan figures supplied for the ratio of beds to population or the number and type of personnel needed must vary from place to place and from time to time, there is a need for more flexibility in planning hospital services and in applying controls to a hospital scheme. The need for beds and personnel will vary with the standard of living. Those with greater incomes are more willing to spend money on health care. In the period 1947 to 1955 in Canada the amount spent on hospital care increased from 1.44% to 2.02% of the net value of national production, though in absolute terms it tripled. When comprehensive hospital insurance is introduced in an area, that part of the population which had the lower income and the greater amount of sickness will avail themselves of more care. Increased use under an insurance scheme arises not so much from abuse as from admissions for the convenience of the patient or his physician, or from inefficient administration. Other factors influencing the need for beds are the increasing complexity of medical science and the change in age composition of the population. The introduction of hospital insurance will affect personnel needs and increase the existing problem of shortages of hospital personnel. Factors influencing the solution of this problem include the increased interest of government, of the insuring agency, and of the public in encouraging training and in recruitment; the increased interest of these bodies in efficient deployment of personnel; and the tendency for employees to demand working conditions and remuneration comparable with those in other fields.

Dr. Kirk Lyon (*Canad. M. A. J.* 78:761, 1958) outlined the challenge presented by the advent of hospital insurance to accrediting bodies. As of Jan. 1, 1959, the Canadian Commission on Hospital Accreditation will be the only body in Canada surveying and granting approval to Canadian hospitals. So far only 50% of hospitals are accredited, most of the nonaccredited ones having less than 150 beds. It is hoped that federal and provincial governments will make no attempt to interfere with this system, for if 10 separate provincial accrediting bodies were set up, the result would be chaotic. Legislation so far proposed permits surveying by the present agency, which is entirely voluntary, but allows the government to step in if it so desires and accredit hospitals. So far provincial governments have shown no sign of disturbing the status quo, but this will depend on the continued voluntary efforts of hospitals and the medical profession to raise the level of hospital care.

In a brief to the federal government the Canadian Association of Medical Colleges recommended: 1. In framing of legislation or regulations there should be safeguards to assure that every school of medicine has hospital teaching units with beds under the control of the faculty of medicine, at the rate of 10 beds for every student in the senior class, at least. 2. A complete outpatient service for diagnosis and treatment in university teaching hospitals should be provided. 3. Governments should recognize the necessity of having teaching units in university hospitals, with physicians appointed by the school as teachers and by the hospital for medical care. It must be made possible to continue the system of graduated responsibility for students. Governments must recognize and accept the fact that such teaching units will cost more than nonteaching units. Numbers of beds must not be determined purely on local needs. 4. If new teaching hospitals or additions to existing ones are planned, larger federal government grants must be made available to provide both outpatient and inpatient facilities.

Occult Uterine Bleeding.—Hurtig (*Canad. M. A. J.* 78:681, 1958) investigated occult uterine bleeding by studying the menstrual cycle in 80 healthy volunteers through 254 cycles. He defined occult bleeding as any bleeding occurring without the patient's knowledge at least 24 hours after menstrual bleeding ceased to be detectable and 24 hours before the onset of the next menstrual period. The significance of such bleeding is that it may be associated with ovulation and could furnish a guide to ovulation behavior in any woman and therefore to contraception by the rhythm method. The practical and simple method developed, by which the volunteers mailed vaginal tampons to a testing laboratory, could also be used for studying sterility, early ulcerative lesions, bleeding corpus luteum, nidation of the fertilized ovum, and ectopic pregnancy. Results suggested but did not prove that occult bleeding comes from the ovary and follows by hours the rupture of the graafian follicle. The study was not extensive enough to warrant any conclusions as to the use of the method for determing the so-called safe period. Complete absence of positive tests suggested sterility with closed tubes, whereas in seven sterile women with proved tubal patency occult bleeding occurred. In some cycles there was a double episode of bleeding, suggesting a possible double ovulation. In all nine pregnant women, isolated early occult bleeding episodes were observed, possibly associated with implantation of the trophoblast.

Abdominal Pain of Cerebral Origin.—Search of the literature reveals some confusion about the occurrence of abdominal pain of cerebral origin in children. Prichard (*Canad. M. A. J.* 78:665, 1958) reviewed a series of 19 patients in whom there was a high degree of probability that abdominal pain was due to a cerebral condition. In 17 children attacks of pain lasted for an hour or more, associated with vasomotor disturbances, nausea, vomiting or headache, drowsiness, and often a family history of migraine and at the most a mild generalized dysrhythmia in the EEG (abdominal migraine), and in two children attacks lasted 5 or 10 minutes sometimes associated with confusion, vasomotor disturbances, nausea, and vomiting. In the latter group a family history of migraine was not characteristic and the EEG showed temporal discharges. These were thought to be cases of true abdominal epilepsy.

INDIA

New Research Facility.—The new research building of the Armed Forces Medical College in Poona was opened in March. The college was opened in 1948 for the training of medical officers of the armed forces. It represents the merger of old Army institutions such as the Medical Training Center, the Research Organization, the Pathology Laboratory, the Transfusion Center, and the School of Radiology.

Lymphangioplasty for Filariasis.—U. M. Rao (*Indian J. Surg.* 20:1 [Feb.] 1958) modified Handley's lymphangioplasty in patients with filariasis, using nylon strands instead of silk. In the initial stages of lymphedema, the superficial lymph capillaries show a marked dilatation with widening of the tissue spaces due to edema. Later there is excessive development of fibrous tissue in the subcutaneous region and fibrotic thickening of the dilated lymphatics. The operation aims at draining the lymph from the dilated lymphatics and tissue spaces in the subcutaneous tissue of the diseased limb into a lymphatic field where drainage is free. This is done by carrying long strands of nylon subcutaneously from the infected extremity across the groin into the subcutaneous tissues of the upper portion of the abdominal wall and the lower portion of the chest. This procedure was performed on three patients, while in three others in whom there was an excess of hyperplastic filarial subcutaneous tissue, the nylon lymphangioplasty was combined with excision of filarial tissue. The 11 patients with only lymphangioplasty experienced immediate subjective relief after the operation, and the limb showed fast shrinkage in the postoperative period, but the size of the limb never returned to normal. Late results showed that the initial improvement was maintained only in three patients. In the three advanced cases where excision was combined with lymphangioplasty, good results were obtained in two while the third continued to have repeated attacks of fever, with painful swelling of the extremity and heaviness and discomfort in the affected limb.

Palpation of Postpartum Uterus.—M. D. Adatia (*J. Indian M. Profession,* May, 1958) stresses the importance of bimanual examination of the uterus after delivery to detect retention of blood clots, placental debris, membranes, or decidua. The author made this examination in 200 postnatal patients and compared the results with a control series of another 200 who were not subjected to such an examination. The bimanual examination was done on the 10th day after delivery, and if the uterus was found to be bulky or not well contracted the uterine cavity was explored with a curved ring forceps. The retained tissues could be easily caught and withdrawn to empty the contents and clear the cavity. The 200 trial patients were watched during their hospital stay for abnormal flow of blood, fever, or any other abnormal sign. In the trial series 38 patients had a single elevation of temperature in the first 48 hours, but this was considered normal; 14 had more than one such elevation, the cause being mastitis in 7, retained products in 4, respiratory infection in 2, and cystitis in 1. In the control series, fever was observed in 18. Ten and 9 patients in the trial and control series, respectively, had irregular bouts of bleeding during their stay in hospital, while 9 and 27 patients, respectively, in the two series complained of irregular bleeding after going home. Fragments of placenta or membranes were removed with ring forceps from 22 patients of the trial series. Of these, fragments in 10 were detected by abdominal examination or the patient noting deficient lochia and complaining of increased pelvic pain. There was no associated rise in temperature, but irregular bleeding was present. In the trial series 158 and in the control series 118 patients started regular menses within three to six months. Abnormal bleeding was observed in 30 patients in the trial and 68 in the control series. Lochia after discharge from hospital was normal in 144 patients in the trial series and in only 66 in the control series. The author believed that removal of retained products reduced the quantity and duration of discharge from the uterus which otherwise caused irregular bouts of bleeding in 68 patients in the control group. This procedure did not affect the onset of menstruation.

Vascular Anastomosis.—Sachdeva and Talwar (*Indian J. Surg.* 20:1 [Feb.] 1958), using dogs, compared different methods of vascular anastomosis. Continuous over-and-over stitch (noneverting with end-to-end approximation) was employed in seven; continuous mattress stitch (everting with intima-to-intima approximation) was used in seven; and alternating interrupted horizontal mattress and simple single stitches (everting with intima-to-intima approximation) was used in seven. The aorta below the renal arteries was divided between two Pott's coarctation clamps. A small portion of the cut ends was denuded of adventitia, the ends were approximated and sutured by one of the three methods, and the clamps were removed. No anticoagulants or antibiotics were used. Patency of the anastomosis in the postoperative period was judged by the presence of femoral pulsations. The dogs were killed after varying intervals and the anastomotic area studied for any dehiscence, hemorrhage, or thrombosis, and sections were made for histological study. Complications were seen in 9 of the 21 dogs; 6 showed thrombosis, which was massive in 3, completely occluding the lumen and leading to postoperative paraplegia. Delayed fatal hemorrhage occurred in two and retroperitoneal hematoma without dehiscence of the anastomosis in two. The six dogs who developed thrombosis comprised two from each group, but the extent of the thrombosis varied, massive thrombosis occurring with the methods in which some suture material presented in the lumens in groups 1 and 3.

Immediate hemorrhage was not usually serious in these animals, but delayed hemorrhage was found to be due to the sutures cutting through, leading to dehiscence and fatal hemorrhage. This occurred with continuous over-and-over stitch in one dog on the fourth day and with continuous mattress stitch in another dog three days after the anastomosis. Retroperitoneal hematoma occurred in two; one with continuous over-and-over stitch and another with continuous mattress stitch. There was no dehiscence of the anastomosis, and femoral pulsations were present when the dogs were killed. On the whole, complications were maximum, with continuous over-and-over (noneverting) suture piercing all the layers. Massive thrombosis, leakage at the time of operation, and delayed hemorrhage were more frequent. Complications were somewhat less frequent with mattress sutures. The authors found the continuous mattress suture satisfactory and reliable. In the third group, where alternating interrupted horizontal mattress and simple single stitches were used, good results were also seen but the procedure was more time-consuming and more likely to cause thrombosis than the continuous mattress suture. Thus the continuous mattress (everting) technique was found to be the best of the methods studied.

JAPAN

Blood Bank.—During a crucial phase of the Korean war fresh blood was urgently needed. Thousands of Japanese donors gave their blood gladly. This did much to overcome an ancient superstition against this practice. This was the beginning of permanent blood banks as they now exist in 32 leading cities throughout Japan. When the banks were organized in 1951 they were able to collect only 3,200 pints of blood. In 1957, however, they reached a peak of 452,000 pints, but because of a growing demand this figure falls short of the annual need by about 168,000 pints. There are about 134,000 professional donors, each of whom gives 200 cc. of blood at a sitting and is paid at a rate of about one cent per cubic centimeter. Because of a tendency to contribute too often about half of the donors have developed secondary anemia. Efforts are being made to recruit a new army of donors. The new donors are being placed in a separate category and are given a deposit slip for each donation which is primarily designated for the use of their own family or friends.

Tissue Bank.—Laws enacted about 60 years ago making it a felony to mutilate the dead in any way have been modified so that the dying may now will any part of his body to be used for humanitarian purposes. This paved the way for the establishment of a corneal bank. Already many blind persons have benefitted. Best results are obtained when the operation is performed within 24 hours from the time of the donor's death. Banks for bones, ligaments, and tendons have also been set up.

Milk Bank.—Practically all babies in Japan are breast fed. Complementary feeding with cow's milk is resorted to only when the mother's milk supply is inadequate. Not infrequently in such cases the infant develops urticaria or asthma due to allergy. To combat such complications in the metropolitan area the government has established a milk bank. The breasts of mothers with an overabundant milk supply are pumped and the milk distributed to needy and allergic victims. Many lives have thus been saved.

UNITED KINGDOM

Retirement for Physicians.—Under the National Health Service physicians in the hospital service and general practitioners (those in the public health service are pensionable under the provisions of the Local Government Superannuation Acts) become eligible for a pension after 10 years' service provided they have also reached the minimum retiring age of 60. Pensionable age is 65. That is the age at which contributions normally cease unless employment is extended. In no case is service after the age of 70 reckonable for pension, and the same applies to service in excess of 45 years. General practitioners may, if they wish, apply to have their pensionable age extended to any age up to 70. Application has to be made after the age of 60 but before 65. If extension is granted, they will continue to pay contributions and reckon service until the extended age or earlier retirement. A general practitioner need not retire at any particular age and may continue to practice in the National Health Service after he has reached pensionable age. He cannot, however, qualify for any extra pension. If he retires on pension at the age of 65 and subsequently goes back on the list of an executive council, he may draw both pension and remuneration up till the age of 70. After he has reached the age of 70 his pension will be suspended or reduced by the amount his remuneration plus pension exceeds the average of the remuneration on which his pension was calculated when he retired.

A general practitioner's pension is calculated as 1.5% of his total "superannuable remuneration" during the last 45 years of service or the whole period of service if less than 45 years. Thus the pension of a doctor retiring in July would be 1.5% of his total superannuable remuneration over the 10 years since the health service started. In addition to the pension there is a lump-sum retirement allowance of 1.5% of the total superannuable remuneration for a married man (whose widow, should he die, would receive a widow's pension) and 4.5% for a single man. In the case of a widower the lump sum would be somewhere between 1.5 and 4.5% of the superannuable remuneration according to the length of time he has been a widower. A widow's pension, generally speaking, amounts to 33% of her husband's pension.

Consultants and senior hospital medical officers are referred to in the scheme as specialists. Part-time specialists' pensions and lump-sum retirement allowances are calculated in the same way as those of general practitioners, but the pensions and retiring allowances of full-time specialists and other full-time hospital officers are calculated on the average of their remuneration during their last three years of service. Their pension is 1/80 of average remuneration for each year of contributing service up to a maximum of 45/80. The lump sum is 1/80 of average remuneration for each year of contributing service up to 45 years for a married man (whose wife is eligible for a widow's pension) and 3/80 for a single man.

Refusal to See Striker.—The Minister of Health was asked in the House of Commons what disciplinary action he proposed to take against a dentist who refused to treat a bus worker because he was on strike. The patient was William Thorndycraft, a maintenance fitter. His wife said that in the week before the strike an appointment was sought and given. This was unsuitable, as her husband had expected to be at work. On the day after the strike started, she telephoned for an appointment in place of the one made for the previous day. The dentist said he wanted nothing to do with the strikers. Mrs. Thorndycraft added that her husband began his vacation two days earlier and had hoped to get an appointment while on vacation. The dentist said that Mrs. Thorndycraft told him that as her husband was on strike he had time to attend for treatment. He twice asked if her husband was in pain or needed emergency treatment and was told he was not. The dentist said he would never turn away anyone in pain. He added that no public servant, be he a doctor, a dentist, a bus driver, a policeman, or a member of the armed forces, has the right to go on strike and that he would be glad to see the patient as soon as the strike was over. The Parliamentary Secretary, Ministry of Health, replied to the original query that a dentist in the National Health Service is free to accept or refuse any patient, who can then seek treatment from any other dentist taking part. In such a case as that reported therefore no Ministerial action was required.

Cosmetic Tattooing.—N. C. Lake (*British Medical Journal*, May 10, 1958) said that after car crashes and various operations patients could be given much cosmetic help through the use of tattooing. An instance was a young woman who was given a "Cupid's bow" to replace an irregular scarred lip left by an operation for hare lip. The remote risks involved should not debar proper use of an excellent method of overcoming disfigurements. Sometimes templates are used. If the subject indicated her wishes with a lipstick, a template is fashioned to suit. Eyebrows may be marked with grease-paint to the patient's satisfaction, and the curve can be copied on a template to guarantee accuracy. Beard-stubbling can be imitated in dark-haired men with pallid facial grafts or scars. Nails, painted or otherwise, can be simulated after amputation of the ends of fingers or toes.

For Better Nutrition.—Thousands of Britons are below par because they are not eating the right sort of food, according to British Medical Association nutritional experts. The association's lay magazine, *Family Doctor*, has launched a nutritional campaign with television announcements and newspaper advertisements, but its major effort is the distribution of three million copies of a cook book entitled "More Fun With Your Food" which will be on sale for 14 cents in thousands of grocery stores. The booklet contains over 100 recipes, a fortnight's planned meals, advice on cheap cuts of meat, and illustrations in color. On each page, tucked between the recipes, are such bits of medical advice as "Have a good breakfast. After a small breakfast you are more irritable, less precise in your work, more easily tired;" "Fish and chips are at least as good as lobster thermidor and saute potatoes, and much cheaper;" "It doesn't matter if you drink with your meals. Do it if you like it;" and "Don't let any theories about coronary disease spoil enjoyment of your meals. Enjoy all the fats—in moderation."

Anticonvulsants and Anemia.—Some anticonvulsant drugs cause megaloblastic anemia, but the true incidence of this anemia among epileptics taking such drugs is not known. Hawkins and Meynell (*Quart. J. Med.* 27:45, 1958) therefore studied a colony of

72 epileptics treated with phenobarbital, diphenylhydantoin, and primidone, either alone or in combination. As controls they included 30 nonepileptic mental defectives living in the same colony and 30 members of the hospital staff. A third of the epileptics had a mean corpuscular volume (M. C. V.) of 94 cubic microns or more. That of the healthy controls was 86.6, and that of the nonepileptic patients was 88.6. Of patients receiving diphenylhydantoin and phenobarbital, 45% showed macrocytosis of the erythrocytes. For those receiving phenobarbital alone the figure was 34%, and it was 27% for those receiving diphenylhydantoin alone. Of the patients receiving diphenylhydantoin and primidone 67% had macrocytosis. The blood change was unrelated to the number of fits or nutritional status. There was no indication of vitamin B_{12} deficiency, as the serum vitamin levels of the epileptics were within normal limits, and those with macrocytosis showed no change in the blood findings when given vitamin B_{12}. No abnormalities in folic acid absorption or tissue depletion were found, but when 20 mg. of folic acid a day was given orally for a month to six patients with macrocytosis the M. C. V. values fell.

Drug-induced macrocytic anemia is uncommon in epileptics. Over a period of two years Hawkins and Meynell found only eight cases in 170 epileptics. Six patients were being treated with diphenylhydantoin, and one with primidone and diphenylhydantoin. In four of the eight the anemia was severe. Five responded to vitamin B_{12} and the remaining three to folic acid. The authors suggested that 5 to 10 mg. daily provides sufficient protection. They also stated that the epilepsy improved if the anemia was treated and that blocking of vitamin B_{12} and folic acid was an important factor in lowering the threshold for the cerebral discharge producing the epileptic attack. It seems therefore worthwhile to examine the blood of epileptics receiving anticonvulsants regularly. If the M. C. V. is high and continues to rise, treatment with folic acid as well as the anticonvulsant is needed.

Royal Society Conversazione.—For almost a century the conversaziones of the Royal Society have been a notable annual feature. At this year's conversazione Drs. Burke and Isaacs had an exhibit on interferon, a compound developed in certain virus cultures, which can inhibit the growth of other viruses treated with it. It was isolated from influenza virus by Isaacs and his colleagues at the National Institute of Medical Research. The substance is a protein and a potent inhibitor in vitro of influenza and related viruses. Sir George Pickering and Mr. W. Cooke, of Oxford, demonstrated an ingenious method of estimating the renin in both the glomeruli and the kidney tubules, by using magnetic methods of separation. The intact kidney is perfused through the renal artery with a suspension of magnetic iron oxide, the particles of which are filtered off by the glomeruli. After grinding up the kidney in Locke's solution the suspension is passed in a tube through the field of a powerful electromagnet. The glomeruli are arrested because of the iron oxide they contain, while the remainder, including the tubules, passes on. The two fractions are assayed for their renin content. The concentration is greatest in the glomeruli. Equipment for polar research was demonstrated by Dr. Lewis and Dr. Masterton, of the National Institute of Medical Research. They showed the daily rations put up for the Greenland and Antarctic expeditions. This ration provides 4,000 calories daily, is scientifically packaged, and is pleasant to the taste. Another polar exhibit showed underwear knitted from plastic-covered copper wire. If connected to a battery it warms the body, and attached to a thermometer it measures skin temperature.

Hyperbilirubinemia of Infants.—In the first two weeks of life a raised serum bilirubin level may lead to kernicterus. The incidence of the signs of this condition increases as the serum bilirubin concentration rises above 20 mg. per 100 ml. The prevention of a high level of serum bilirubin, or its destruction, or its removal from the body, will prevent kernicterus. The condition has hitherto been relieved by replacement transfusion. Cremer and co-workers (*Lancet* 1:1095, 1958) showed that the serum bilirubin of jaundiced infants is highly photosensitive. They found that both bilirubin (van den Bergh indirect pigment) and conjugated bilirubin (van den Bergh direct pigment) are destroyed by white light. The nursing staff observed that the yellow pigmentation of the skin of jaundiced babies quickly faded when they were exposed to sunlight. The authors confirmed this and showed that jaundice quickly disappeared from the exposed skin of the infants but persisted in areas that were covered. After the treatment of premature infants with sunlight their "physiological jaundice" quickly disappeared, coinciding with a rapid fall in the serum bilirubin level. The same effect was produced by exposure to ultraviolet lamps, the drop in serum bilirubin level being proportionate to the period of light exposure. While they do not consider that light treatment will prove a substitute for exchange transfusion in the erythroblastotic infant with active hemolysis, they believe the method may be turned to clinical advantage in controlling the serum bilirubin level in patients with the jaundice of prematurity.

Zirconium Granuloma.—Red-brown papules in the axilla were observed after the use of deodorant sticks containing sodium zirconium lactate. The nature of these lesions was investigated by Shelley and Hurley, (*Brit. J. Dermat.* 70:75, 1958) who stated that the clinical signs and histological changes in the dermis were characteristic. They instructed 30 volunteers to rub a zirconium stick deodorant containing 5% zirconium into one axilla every morning for five minutes, an identical stick, but free of zirconium, being rubbed into the other axilla for the same time. Both axillas were shaved every other day and after ten weeks biopsy specimens were taken from each axilla. Axillary reactions in the form of confluent papules arranged in a linear fashion appeared in the treated axillas of 10 of the volunteers. Microscopically the papules had the appearance of granulomas in the corium, composed of epithelioid cells and giant cells surrounded by lymphocytes in a typical tuberculoid pattern. There was no reaction in the untreated control axillas. Intradermal testing showed a unique granulomatous response, occurring in one subject at a dilution of 1:10,000. The authors concluded that the granulomas were the direct result of a specific allergic hypersensitivity to zirconium. This was the first time the introduction of extremely small amounts of a pure substance has produced an epithelioid granuloma in man. Zirconium has now been withdrawn from use in deodorants.

Streptococcic Infection in Children.—Holmes and Williams (*J. Hyg.* 56:43, 1958) made a long-term investigation of streptococcic disease in about 400 children living in a large home over a period of two and a half years, during which 473 sore throats were studied; 60% of these were infected with the group A streptococci. The monthly attack rate was 1.9 throat infections per 100 children. The incidence increased with the age of the child. Thus the proportion of sore throats yielding streptococci increased from 34% in children aged up to 2 years, to 74% in those over 10. Tonsillectomy had a negligible influence on the severity of the streptococcic infections. Throat carrier rates decreased more rapidly in tonsillectomized convalescent children than in the nontonsillectomized, but the nasal carrier rate was higher in the tonsillectomized children at the beginning of the infection and during convalescence. Of the probable or possible contacts of the affected children 67% were heavy-nasal carriers of streptococci, and the remainder were light-nasal or throat-only carriers. This emphasizes the importance of the nasal carrier as a source of streptococcic infection. No cases of rheumatic fever or acute glomerulonephritis were observed among several hundred patients with streptococcic illness.

Dietary Treatment of Myopic Children.—After an earlier observation that an increase in degree of myopia is greater in undernourished children, particularly those consuming diets low in animal protein, Gardiner (*Lancet* 1:1152, 1958) compared the refractions of two groups of myopic children excluding those known to have congenital myopia; 95 children were given a diet in which 10% of the caloric intake was in the form of animal protein. No attempt was made to alter the usual caloric intake or quantity of food eaten, and free use was made of a preparation of calcium caseinate as a supplement for those who disliked animal protein. The control group was given no dietary advice whatsoever. Changes in refraction in both groups were recorded at intervals over a year. Examination of the results after this time showed that those children who received extra animal protein showed less visual deterioration associated with their myopia than the untreated controls. With a few exceptions, those among the younger children who carried out the treatment most assiduously tended to show deterioration more slowly than those less careful about their protein intake. Of the children over 12, there was improvement in most of those who took the greatest quantity of animal protein. Gardiner concluded that whatever the cause of acquired myopia in children and adolescents, its course could be favorably modified by dietary means. Milk played an important part in the control of myopia, and perhaps some part was played by the vegetable protein intake as well. The balance of the diet and not the animal-protein content might have been a factor, since it was radically changed in the treated group.

Anemia due to Intestinal Bleeding.—Anemia is common in elderly people admitted to hospital whatever their presenting clinical condition. Bedford and Wollner (*Lancet* 1:1144, 1958) showed that occult intestinal hemorrhage can be detected in many of these anemic patients. They examined 156 consecutive patients, aged 65 years or more, with no overt bleeding. Weekly hemoglobin estimations and blood film examinations were made, and at the same time a fresh specimen of feces was examined for occult blood. A hemoglobin level of less than 80% (11.7 Gm. per 100 ml.) was arbitrarily taken to indicate anemia. Of the 156 patients 64, or 41%, were anemic by this definition, 22% having hemoglobin levels below 75% and 13% levels below 70%. The incidence of anemia was similar in all the age groups over 65, and the incidence of anemia in men and women was the same (41%). The occult blood test was positive in 55% of the patients, the incidence of a positive reaction being similar in all the age groups over 65. Of the 64 anemic patients, 78% gave a positive occult blood test, whereas of the 92 with a hemoglobin level of more than 80%, only 38% gave a positive occult blood test. Bedford and Wollner rejected the view that the anemia of old age is physiological. In their opinion the major cause was occult intestinal hemorrhage, with achlorhydria and poor dietary intake of protein and ascorbic acid as contributory factors.

CORRESPONDENCE

DRUG HABITUATION

To the Editor:—In The Journal of February 22, page 881, we were pleased to see that another physician, Dr. Austin R. Stough, has been studying the possibile habituating properties of meprobamate. We were sorry to see that no true controls were used, although placebos were utilized. It seems that the observations of the patients were not conducted by a "blind" observer and that no truly objective evaluation of the patients was made before, during, and after the study, except for physiological measurements. Dr. Stough's paper and conclusions are important, but there are a few points with which we would like to take issue.

In discussing possible habituation to meprobamate, Dr. Stough states that tolerance is absent or minor in habituation and progressively increases in addiction. He states that "no true habituations" to meprobamate developed. It seems to us that he did demonstrate the development of tolerance in his patients. He used steppage dosages of meprobamate and says that the women who received the largest dosage "reported a temporary mild drowsiness at each increase of the dose, but all adjusted as the medication continued." This "adjustment" sounds as if Dr. Stough were observing development of tolerance. He mentions that the women who received 6.4 Gm. daily were, in some cases, unable to operate their sewing machines. This dosage was continued for one week. In our experience, patients receiving 6.4 Gm. daily did develop tolerance after about 7 to 10 days, during which time they were, indeed, showing toxic effects. After this period of time they were able to continue with their daily routine.

Dr. Stough has developed the concept that on withdrawal of meprobamate there is a "resurgence of previous psychosomatic symptoms," apparently based upon the subjective complaints of his patients. In a study of our own, which was a true "double blind" experiment, the observer's check sheets completed before, during, and after the meprobamate administration did not warrant any such conclusion. We wonder if the symptoms which "returned with shocking suddenness" in Dr. Stough's study might not be an indication of a real desire, both physiological and psychological, to resume use of the drug? In addition, surely the grand mal seizures described were not returning but were appearing de novo.

In his summary Dr. Stough states that discomforts occurred "in a small percentage" on withdrawal of meprobamate. However, on the same page he lists the 49 patients in program 1 who received 3.2 or 6.4 Gm. of meprobamate daily. Adding up those instances in which Dr. Stough lists "discomfort in placebo period," we reach a total of 35 patients out of 49. This is 71% of his total number of subjects—surely not a small percentage.

Turning to Dr. Stough's description of some of his patients, one finds the following phrases: "highly nervous," "emotional," "unstable," "unhappy," "frustrated individuals," with "irritability," "central nervous system damage or serious mental, emotional, or character abnormalities." The last phrase describes those who are said to react in an undesirable manner on "abrupt cessation of any type of ataractic therapy." Disregarding the inadequate description involved in these terms, we must point out that these are the very patients for whom meprobamate is prescribed. Surely this drug was introduced for use in psychiatry, and meprobamate is not intended for people without some of these problems.

In any case we must protest Dr. Stough's extrapolation of his meprobamate results to "any type of ataractic therapy." In our opinion meprobamate is clinically much closer to the barbiturates and is less like the majority of presently available ataractics.

Our own results will be published in the *New England Journal of Medicine*. Briefly, in a "double blind" experiment, we were able to show that on abrupt withdrawal of meprobamate, after 40 days of administration of 6.4 Gm. or 3.2 Gm. daily, withdrawal reactions occurred with statistical significance as compared with those in the controls. We agree wholeheartedly that the development of dependence upon a drug involves both psychological and, in the case of active drugs, physiological factors. We feel that the unfortunate fact about meprobamate is that a true physiological dependence does occur. We certainly agree with the need for a slow withdrawal of meprobamate after its administration, but we advocate this not because of "resurgence of previous psychosomatic symptoms" but because of the development of new withdrawal symptoms very similar to those appearing after administration of barbiturates and their rapid withdrawal. In our opinion these withdrawal symptoms may be mistaken by physician and patient alike for psychogenic symptoms, and the patient may wrongly be put back on the tranquilizer instead of merely being withdrawn more slowly.

At the present time further study of meprobamate is continuing here. It is proposed to ascertain if physical dependence can occur at much smaller dosage than that formerly employed, if given over sufficiently large periods of time. In addition, we are studying the rate at which the drug may be withdrawn safely so as to avoid the occurrence of the "abstinence syndrome."

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Malpractice: Failure to Discover Severed Tendon: Res Ipsa Loquitur.—This was an action for damages for injuries alleged to have been caused by negligent emergency treatment rendered by an intern employed by the defendant hospital. From a judgment in favor of the defendant hospital, the plaintiff appealed to the Supreme Court of Delaware.

The plaintiff, 16 months of age, cut her hand severely on a piece of glass and was taken to the emergency ward of the defendant hospital. She was crying and struggling so that she had to be held by her parents and a student nurse then on duty. An intern examined the wound, treated it and sewed it up, and, in response to a question by the infant's father, stated that the tendons of the hand were not severed. Sometime later the plaintiff was again taken to the hospital and was again examined by the same intern. He noted a stiffness in the index finger but made no diagnosis of the possible cause of that stiffness. She was treated at the defendant hospital yet a third time and finally, about three months after the accident, went to another hospital, where she was advised that the tendon serving the index finger had been severed and that an operation would be required to repair it. The operation had not been performed at the time of the trial four years later.

Two doctors testified as experts on behalf of the plaintiff. They said that in a child of 16 months the tendon leading to the index finger is approximately the size of a heavy piece of string. By visual examination of a wound, they said, it is possible to see the tendon if it has not been severed but they admitted that in the case of a small struggling and crying child it is entirely possible that the tendon would not be seen. They pointed out that it is routine practice to determine, if possible, whether or not tendons have been severed, but if the child is uncooperative this is oftentimes impossible to determine, because diagnosis requires flexion of the finger which, in turn, can be achieved only by cooperation of the patient. They testified that when a tendon is severed an operation is required to repair it, since a severed tendon will not grow together of its own volition, but they agreed that an immediate operation is not always performed. In fact, they were agreed that an immediate operation is not necessary and that postponement of the operation even for as long as four years would not result in any permanent disability by reason of the delay. Finally, these doctors testifying for the plaintiff said that it was possible that, at the time of the initial examination by the intern, the tendon leading to the plaintiff's right index finger was only partially severed, which would not have been discovered by examination, and that the tendon might have ruptured later, after the initial treatment.

The Supreme Court pointed out that the sole fact that an injury has resulted from a certain treatment does not raise any presumption of negligence on the part of the attending doctor and that it is therefore incumbent on a plaintiff to prove the medical standards to which the doctor is required to conform. This must necessarily be established by competent expert testimony. It is clear from the plaintiff's witnesses that the intern at the defendant hospital examined the plaintiff as any other doctor in the community would have examined her under like circumstances. There was no evidence that his treatment of the wound and suturing failed in any respect to conform to the established standards for the medical profession. It is also clear that the failure to ascertain immediately the severing of the tendon did not result from a failure to conform to the accepted standard and, in any event, that no permanent injury has followed the failure to discover the condition.

The plaintiff, however, contended that the issue of negligence should have been submitted to the jury because of the doctrine of res ipsa loquitur. The Supreme Court said that in order to determine the availability of the doctrine the court must examine the manner in which the alleged injury occurred and then determine whether or not in the usual course of events it would be concluded by reasonable persons that the injury would probably not have occurred except for some negligence on the part of the defendant. This case, continued the court, in its best light for the plaintiff is, at most, one of an unfavorable result from the treatment employed. It seems clear in such circumstances that, on the basis of the unfavorable nature of the result of treatment, no presumption of negligence on the part of the doctor can arise. It could not be concluded that the injury would probably not have occurred except for some negligence. We are of the opinion, therefore, that the trial court was correct in refusing to submit the issue to the jury on the doctrine of res ipsa loquitur. The judgment in favor of the defendant hospital was therefore affirmed. *Christian v. Wilmington General Hospital Association,* 135 A(2) 727 (Del., 1957).

MEDICAL FILM REVIEWS

Medical Aspects of High Intensity Noise: General Effects: (MN 9318-a): Medical Aspects of High Intensity Noise: Ear Defense (MN 9318-c): 16 mm., black and white, sound, showing time 21 minutes each. Produced in 1956 by the De Frenes Co. for the Department of the Navy. Procurable on loan from Audio Visual Training Section, Bureau of Medicine and Surgery, Department of the Navy, Washington 25.

These two films point out the hazards associated with high noise levels produced by jet aircraft and other noisy equipment found on shore and aboard ship. They describe the nature of noise and some of its physiological and psychological effects. Various devices that are used for the protection of hearing are shown. A good review of the fundamentals of sound conduction is also included. The presentation of the problem is dramatic and effective. The films are beautifully done from the technical standpoint. Although they were made especially for training navy personnel, they could also be used in the airplane industry and can be recommended to any audience interested in a fundamental presentation of the basic effects involved in the noise problem.

That the Deaf May Speak: 16 mm., color, sound, showing time 42 minutes. Produced in 1952 by Campus Film Productions, New York, for the Lexington School for the Deaf, New York. Procurable on loan from Ideal Pictures Corp., 58 E. South Water St., Chicago 1.

The problems faced by the deaf in a hearing world are told in this film, which also shows the terrible impact on parents of the discovery of deafness in their child. The development and training of the death child from the moment of entry into the Lexington School through the years of nursery and preschool and finally on through the eighth grade is traced. Emphasis is on the advancement in speech and language made by the children. This is a good film for recruitment of teachers and also for general information. The photography is excellent. It is recommended for otologists and general practitioners as a means of informing parents of deaf children about the facilities for training these children. It would also be of interest to parent-teacher organizations, vocational guidance counselors, and rehabilitation groups.

The Months Before Birth: 16 mm., black and white, sound. Produced in 1956 by KQED, Pittsburgh, for the Educational Television and Radio Center, Ann Arbor, Mich. Procurable on rental from Indiana University, NET Film Service, Audio Visual Center, Bloomington, Ind.

This series of eight half-hour kinescoped television programs is designed especially for the expectant mother. It shows the anatomy and physiology of reproduction, the development of the baby, the processes of birth, and the care of the mother during the months of pregnancy. In the last program the weeks after birth are discussed. An effort is made also, through these films, to dispel some of the old fears and superstitions surrounding pregnancy. This film series consists mainly of lectures given by Dr. Anna Wagner, Chief of Maternal and Child Health of the Pittsburgh Department of Public Health. Although Dr. Wagner employs only a minimum number of visual aids, she presents the information in an interesting manner. The lecture technique varies throughout the series, from the use of a small class to introduce the type of questions which might be asked by the inexperienced expectant mother to an interview of consultants who are specialists in the subjects discussed. The eight programs in this series are as follows: (1) The Physiology of Reproduction, (2) The Beginning of Pregnancy, (3) The First Visit to the Doctor, (4) Nutrition and Dental Care in Pregnancy, (5) The Middle Months of Pregnancy, (6) The Last Months of Pregnancy, (7) The Birth of the Baby, and (8) The Weeks After Birth. These films are recommended for expectant mothers and for medical personnel who are asked to lecture on certain stages of pregnancy.

Exenteration of the Orbit: 16 mm., color, sound, showing time 23 minutes. Prepared by Algernon B. Reese, M.D., New York. Produced in 1957 by Sturgis Grant Productions, New York. Procurable from American Cancer Society, Inc., 521 W. 57th St., New York 19.

The purpose of this film is to demonstrate two slightly different techniques for exenteration employed by the author, in connection with two orbital tumors, to show results achieved as well as various methods used by patients to conceal the resulting defects. The first case is an exenteration for a malignant epithelial tumor of the lacrimal gland. Incisions are made below the lower lid margin and above the upper lid margin, the lids having been sutured together. Dissection is carried beyond the orbital margins, canthal ligaments are severed, and the periosteum is separated in all quadrants of the orbital wall. After final dissection, the orbital contents are removed. In this case a Thiersch graft is used to cover the bony orbital wall, inserted with the aid of a tampon. The second case is an exenteration for rhabdomyosarcoma of the orbit. Here, the upper and lower lids are first halved, and the interior half of each lid is undermined to the orbital margin. In this case, after orbital contents are removed the temporalis muscle is mobilized, passed through an opening made in the lateral bony wall of the orbit, and used to fill the defect. No graft is used, the upper and lower lid margins being sutured together to effect closure of the wound. End results comparing the two techniques are shown, and a review of various devices from shields to prostheses are demonstrated beautifully. The photography is excellent, and the film is highly recommended for ophthalmic surgeons.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Congenital Cystic Disease of the Lung with Progressive Pulmonary Fibrosis and Carcinomatosis. V. A. McKusick and A. M. Fisher. Ann. Int. Med. 48:774-790 (April) 1958 [Lancaster, Pa.].

The authors report on 2 brothers, aged 32 and 37 years, and on a 53-year-old man with hereditary miliary bronchoalveolar cystic disease. The younger of the 2 brothers was admitted to hospital because of dyspnea, occasional orthopnea, and palpitation for the preceding 3 years. His fingers had been clubbed since the age of 18 years. There was no definite evidence of heart failure. Chest roentgenograms revealed considerable increase in the size of the heart and diffuse pulmonary fibrosis bilaterally. There was increased prominence of the pulmonary artery. The blood pressure was 106/60 mm. Hg. The patient died of cor pulmonale, and autopsy was not performed. Clinically, no basis was found for the pulmonary hypertension other than progressive, diffuse pulmonary fibrosis, the causation of which was not clear. The older brother was admitted to hospital because of shortness of breath. He died at the age of 40 years after a progressively downhill course of several years' duration, manifested by radiologic evidence of diffuse and progressive pulmonary fibrosis, pain in the fingers and toes, which had been clubbed most of his life, and respiratory failure of the alveolocapillary block type. Autopsy was performed and revealed cysts of the lung, probably congenital, extensive fibrosis, and carcinomatosis of pulmonary origin. The third patient had clubbing of his fingers all his life, and his chest roentgenograms showed progressive pulmonary fibrosis over a period of 10 years. Weight loss and severe respiratory failure were striking features in the last months of life. Autopsy revealed numerous cysts of the lung, lined with bronchial epithelium which in places was mucus secreting; smooth muscle strands were present in their walls. These findings satisfied the usual criteria for congenital cysts. A large tumor mass had destroyed the wall of the bronchus of the upper lobe of the right lung and projected into it. The tumor was squamous-cell carcinoma.

There is a variety of congenital cystic disease of the lung which is genetically determined. The pulmonary lesions may be completely silent and resistant to clinical detection for many years. However, clubbing of the fingers and toes or more advanced forms of hypertrophic pulmonary osteoarthropathy may develop many years before subjective or objective pulmonary signs. The diffuse miliary variety of congenital cystic disease of the lung is likely to give rise to progressive, generalized pulmonary fibrosis with cor pulmonale and/or the syndrome of alveolocapillary block. Carcinomatous degeneration occurs as another late complication.

The Clinical Picture of Far East Influenza Occurring at the Fourth National Boy Scout Jamboree: Report of 616 Cases. R. L. Podosin and W. L. Felton. New England J. Med. 258:778-782 (April 17) 1958 [Boston].

The occurrence of an epidemic of Far East influenza at the 4th National Boy Scout Jamboree, held at Valley Forge, Pa., from July 12 to 19, 1957, enabled the authors to study the clinical aspect of the disease in 616 patients. To establish the causation of the epidemic, viral isolation and serologic studies were carried out on 31 representative patients, in 13 of whom hemagglutinating agents identified as the virus of Far East influenza, type A, 1957, were recovered. In addition, paired serums from 9 patients showed significant rises in antibody titer against the Far East strain. Of the 616 patients, 591 were boy scouts, between the ages of 11 and 19 years, and 25 were adult leaders. Pharyngitis, rhinitis, and conjunctivitis represented a part of the primary viral infection. The most consistent finding was fever which was seen in 95% of the patients at some time in their course, the average highest recorded temperature being 102.1 F (39 C). Gastrointestinal symptoms were marked in 42 patients. The course of the disease in 98 patients (15.9%) was complicated by pneumonitis, otitis media, acute tonsillitis, or acute bronchial asthma. No serious sequelae occurred in these patients. Ninety-four per cent of the patients were in the hospital for 4 days or less, but older patients and those with acute asthmatic attacks had a slightly prolonged course and a higher rate of pulmonary complica-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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tions. Antibiotic therapy was not utilized; it does not appear to be indicated in the uncomplicated case and should be reserved for patients with pneumonitis or other obvious bacterial complications.

Results of Skin Testing in Military Personnel. I. L. Bernstein and J. Schwarz. Ann. Int. Med. 48:791-796 (April) 1958 [Lancaster, Pa.].

All personnel, officers and men, of the Wurtsmith Air Force Base were tested between Jan. 19, 1953, and Feb. 18, 1953, with purified protein derivative (first and second strengths), histoplasmin, blastomycin, and coccidioidin antigens. Each person tested received 0.1 cc. of each of the above antigens intradermally on forearm sites, and these areas were read 48 hours later. Indurated areas of 0.5 mm. or more were considered positive. In this heterogeneous military group, 10% reacted to tuberculin and 18% to histoplasmin. Teleroentgenograms were taken from all positive reactors. Pulmonary calcifications were observed with greater frequency in the histoplasmin-positive group. Many of these calcifications were located in the hilar regions, and considerable numbers of these were 1 cm. or larger in size. Evaluation of parenchymal and hilar calcifications should always include histoplasmin skin testing. The benign nature of such lesions should also be stressed, inasmuch as the persons tested presented a random sampling of healthy men. Cross sensitization between histoplasmin and blastomycin was also observed in this military group; this emphasizes the need for careful evaluation of a blastomycin skin reaction.

Long-term Combined Drug Therapy in Non-malignant hypertension. H. Stürup and A. Grüner. *Acta med. scandinav.* 160:251-260 (No. 3) 1958 (In English) [Stockholm].

The authors report on 75 patients with nonmalignant hypertension, all of whom had a diastolic blood pressure, averaging at least 110 mm. Hg before the institution of treatment, and retinal, cardiac, renal, or cerebral complications. The patients were treated with various combinations of reserpine (Serpasil), hydralazine (Apresoline), and pentolinium (Ansolysen) given by mouth. Four patients died within 6 months, 3 of apoplexy and 1 by committing suicide. Seven patients did not cooperate, and 13 have not yet been treated for 6 months. The remaining 51 patients were treated for from 6 to 30 months. A sustained, unequivocal, satisfactory drop in blood pressure was obtained in 26 patients; in 10 this result was obtained with reserpine alone, in 7 with combined administration of reserpine and hydralazine, and in 9 with combined administration of all 3 drugs. The average drop in blood pressure in the 26 patients was 35 mm. Hg, corresponding to a drop from 220/127 mm. Hg to 175/97 mm. Hg. In the 25 patients with an unsatisfactory response to the treatment, the average drop in mean pressure was 17 mm. Hg, corresponding to a drop from 219/129 mm. Hg to 202/112 mm. Hg. The patients with a satisfactory response and those with an unsatisfactory response to the treatment were identical with regard to sex, age, and pretreatment level of blood pressure. The duration of treatment averaged 21 months in the group with a satisfactory response against 14 months in that with an unsatisfactory response. Retinal hemorrhages and exudates disappeared in 13 of 14 patients, regardless of whether the treatment resulted in a satisfactory or an unsatisfactory fall in blood pressure. The number of patients with a negative T_1 wave in the electrocardiogram was reduced from 9 to 3 in the group with a satisfactory response to treatment but remained unchanged in the group of 14 patients with an unsatisfactory response. The number of patients with albuminuria was reduced from 11 to 2 in the group with satisfactory results and from 10 to 8 in the group with unsatisfactory results. There was no significant reduction in the size of the heart. One of the 51 patients died of uremia. One patient had an attack of apoplexy associated with hemiparesis. Coronary thrombosis or congestive heart failure did not occur. Treatment still continues in 47 patients.

The Effect of Tilting on the Right Atrial Pressure of Patients with Heart Failure. J. M. Ryan, B. M. *Oser and J. R. Huston. Am. Heart J.* 55:656-661 (May) 1958 [St. Louis].

Twenty-seven patients, 9 with a normal heart, 7 with clinical evidence of heart disease, and 11 with advanced heart failure, were placed in the recumbent position; a cardiac catheter was passed into the right atrium, and the atrial pressure was determined with the catheter connected to a sodium chloride solution manometer. The patients were then tilted vertically to 90 degrees and were unsupported, and the atrial pressure was determined again in the upright position. Repeat determinations of the atrial pressure in both the recumbent and the upright position were made in 6 of the 11 patients after treatment of their heart failure. The 9 patients with a normal heart and 4 patients with clinical evidence of heart disease had recumbent right atrial pressures of 115 mm. or less of sodium chloride solution, averaging 83 mm. of sodium chloride solution. On assuming the upright position, the average reduction of this pressure was 88 mm. of sodium chloride solution. Three patients with heart disease had recumbent right atrial pressures ranging from 115 to 160 mm. of sodium chloride solution; in this group the average orthostatic decrease in pressure was 102 mm. of sodium chloride solution. The 11 patients with advanced heart failure, who had recumbent pressures of over 200 mm. of sodium chloride solution, had an average pressure drop of 161 mm. of sodium chloride solution after tilting. The average time required for stabilization after tilting in those with recumbent atrial pressures below 115 mm. of sodium chloride solution was 12.3 minutes, while that in those with pressures above 200 mm. of sodium chloride solution was 13.5 minutes.

There appears to be direct correlation between the height of the recumbent right atrial pressure and the total fall of this pressure when the patient is tilted to the vertical position. The higher the right atrial pressure during recumbency, the greater the pressure fall after vertical tilting. When treatment of heart failure was successful in restoring high recumbent atrial pressures to the normal range, the reductions in these pressures after tilting were then of the same magnitude as in normal patients. The factors thought to be responsible for these findings and also the possible relationship of these observations to orthopnea are discussed. It would appear that in congestive failure the venous system can be still further distended in the lower part of the body when the venous pressure in that region is increased on the assumption of the erect posture. The resultant blood trapping, with displacement of blood away from the heart, would lower the intracardiac pressure by reducing intracardiac blood volume. One would expect increased movement of fluid out into the tissues when the venous pressure in the lower half of the body increased after tilting. This too would reduce the blood volume, some of which would be intracardiac, and cause a lowering of the right atrial pressure. Another factor to be considered is that displacement of blood away from the heart after tilting increases the cardiac output of those patients with congestive failure and thus reduces the atrial pressure. The functional residual capacity of the lungs is greater in the upright than in the recumbent position and is accompanied by a further lowering of the negative intrathoracic pressure. This additional reduction of the pressure in the thorax undoubtedly accounts for a portion of the change observed in the atrial pressure after tilting.

The Question of Incidence and Cause of Gastric and Duodenal Ulcers in the Presence of Organic Peripheral Circulatory Disturbances. E.-G. Preuss and G. Heidlemann. München. med. Wchnchr. 100:625-627 (April 18) 1958 (In German) [Munich, Germany].

The authors emphasize that it is of diagnostic, therapeutic, and prognostic importance that organic disturbances in the peripheral circulation be regarded not as isolated vascular disturbances but rather as having a tendency to systemic generalization. This applies to endangiitis obliterans as well as to arteriosclerosis obliterans. These 2 processes cannot always be differentiated, mixed forms having been demonstrated histologically. On investigating the histories of 416 hospitalized and 2,345 ambulatory patients with obliterating disorder of the arteries of the extremities, the authors found that 20.7% of the hospitalized and 13.4% of the ambulatory patients had histories of gastric or duodenal ulceration. This relationship between peptic ulceration and peripheral organic vascular diseases had been reported by other observers on smaller numbers of patients, but the percentages were even higher. The authors feel that a high incidence of peptic ulceration in the presence of organic vascular diseases can now be regarded as statistically proved. The gastrointestinal ulceration appears in about 75% of the patients from 10 to 20 years before the peripheral vascular disturbances. It is believed that the factor common to both conditions is a constitutional tendency to arteriolar constriction (angiopathic reaction). This is not the only factor, however, for additional sex-linked factors play a part.

The Significance of Rectal Bleeding in Diverticulosis and Diverticulitis of the Colon. R. A. Scarborough. Dis. Colon & Rectum 1:49-52 (Jan.-Feb.) 1958 [Philadelphia].

During the past 12 years, a malignant or a premalignant tumor (adenoma) of the large intestine was removed from 89 patients who had been observed for more than 1 year previously and in whom a diagnosis of diverticulosis or diverticulitis had been accepted as the cause of gross rectal bleeding. The average length of observation was 2.3 years. The author excluded from the series all patients who had diverticular disease and bleeding due to other established causes, including hemorrhoids and fissure-in-ano, and all patients with diverticular disease in whom diagnosis of neoplasm was made in less than 1 year. The 89 patients ranged in age from 40 to 80 years; 55% were men, and 45% were women. The majority of patients had noted repeated episodes of small to moderate amounts of bright or dark red blood on or in the stools. Eight patients had passed large clots of blood. Five patients had episodes of moderately severe bloody diarrhea. Six patients had 1 or more episodes of profuse amounts of red blood not requiring transfusion or hospitalization. There were 5 patients who gave a history of severe hemorrhage, necessitating hospitalization and multiple transfusions 2 to 4 times during the previous 1 to 3 years.

During the same period the 89 patients were observed, only 16 patients were observed who proved to have bleeding from diverticulitis and 8 others had diverticula. In the author's experience, rectal bleeding which might have been considered attributable to diverticulosis or diverticulitis of the colon has ultimately been proved to have been due to neoplastic disease 4 times out of 5. Diagnostic procedures in case of rectal bleeding should include a history to ascertain the characteristics of bleeding. Anoscopic examination should always be done to evaluate adequately internal hemorrhoids or a possible fissure-in-ano as the source of bleeding. Thorough sigmoidoscopy is required for evidence of neoplastic or ulcerative disease or for evidence of blood coming from above the level of the examination. Only after the preceding steps have been taken should roentgenologic examination of the abdominal portion of the colon be performed. This examination should be particularly thorough when diverticula are found, because in such instance the demonstration of a polyp or of a carcinoma is often especially difficult. When the character of bleeding has been such that it could have come from higher in the gastrointestinal tract, roentgenologic examination of the stomach and small intestine should be done. When roentgenologic examinations show only evidence of diverticula, and the patient has repeated evidence of blood coming from above the rectum, exploratory laparotomy and colonoscopy of the entire colon is recommended.

Problem of the Interrelationship of the Increase in the Serum Lipid Level and the Constitution and Age in Patients with Arteriosclerosis. E. Boehle, R. Biegler and G. Hohnbaum. Medizinische 16:664-669 (April 19) 1958 (In German) [Stuttgart, Germany].

The authors report on 513 patients with arteriosclerosis admitted to the first medical clinic of the University of Frankfort on the Main between 1954 and 1957. There were 452 men and 61 women. Three hundred twenty-one men, between the ages of 34 and 79 years (average age, 56 years), had sclerosis of the coronary arteries; 71 men, between the ages of 61 and 82 (average age, 64.1 years), had sclerosis of the cerebral arteries, and 60 men, between the ages of 33 and 71 (average age, 55.8 years), had peripheral sclerosis. The 61 women were between the ages of 41 and 86 years (average age, 62.6 years). Because of the relatively small number of women with vascular disease, a subdivision according to the various arteriosclerotic processes, similar to that for men, was omitted. Most of the patients with sclerosis of the coronary arteries showed a significantly increased level of serum lipids, the average value of total lipids being 1,086 mg. per 100 cc. These patients were of the pyknic-athletic type, relatively young, and with a tendency to obesity. Most of the patients with sclerosis of the cerebral arteries were of the leptosome type, of advanced age, and the level of their serum lipids was not significantly increased, the average value of total lipids being 934 mg. per 100 cc. Most of the patients with peripheral arteriosclerosis were less advanced in age; constitutional symptoms and the level of their serum lipids were similar to those of patients with cerebral arteriosclerosis. The women with arteriosclerosis were mostly of the pyknic type; the level of their serum lipids was significantly increased, the average value of total lipids being 1,028 mg. per 100 cc. These patients were of comparatively advanced age.

These data suggest that changes in the serum lipid level are the expression of constitutional characteristics, of age, and of peculiarities of metabolism of the patients. It must, however, be admitted that exogenous causes, such as high intake of fat and rich caloric food, favor the occurrence of arteriosclerosis in man, although constitutional factors may also play a part.

Tuberculin Sensitivity in the Middle-aged and Elderly. M. Caplin, P. Silver and W. F. Wheeler. Tubercle 39:84-89 (April) 1958 [London].

A Mantoux test survey with purified protein derivative of tuberculin (tuberculin P. P. D.) in increasing doses was carried out on 201 male and 279 female nontuberculous subjects and on 149 male and 20 female tuberculous patients, all over 45 years of age and all residents of London. Dilutions of tuberculin P. P. D. were used, starting with 1 tuberculin unit (T. U.) (0.1 ml. of 1 in 10,000 dilution) and proceeding, if the reaction proved negative, to 10 T. U., 100 T. U., and finally 1,000 T. U. (0.1 ml. of 1 in 10 dilution). A positive reaction to 1 T. U. revealed those with the highest sensitivity. This was found in 60% of the men and 39% of the women, over 45 years of age, who were free from tuberculosis. For those under 65, the respective figures were 79 and 60%, and for those over 65, 50 and 32%. There was a gradual decline with age, and in each age group the percentage of positive reactors was higher in men. With the 1,000 T. U. test, 98% of the men and 95% of the women were positive. Intrapulmonary calcification was found in 34% of 164 nontuberculous men and 21% of 235 women. No relationship could be found between calcification and tuberculin sensitivity. Four of the 19 patients negative to 1,000 T. U. showed intrapulmonary calcification as evidence of old healed tuberculosis. In the tuberculous men, a positive reaction to 1 T. U. was obtained in 96%, there being slight decline with age; only 1% failed to react to 10 T. U., less than 1% to 100 T. U., and none to 1,000 T. U.

A Type of Cushing's Syndrome Which Developed After Administration of Prednisone for Miliary Tuberculosis. M. Abrate and P. Cavallero. Minerva med. 49:693-696 (Feb. 24) 1958 (In Italian) [Turin, Italy].

The authors report on the fatal case of a 16-year-old girl with miliary pulmonary tuberculosis, in whom administration of small doses of prednisone caused grave Cushing's syndrome-like signs, similar to those which develop after administration of high doses of cortisone for a prolonged period of time. The first 20-day treatment with streptomycin (1 Gm. a day) and isoniazid (300 mg. a day) brought no result. The subsequent 10-day treatment with prednisone (20 mg. a day) and isoniazid (200 mg. a day) brought about improvement in the meningitic symptoms, body temperature, Katz index, and roentgenologic picture. Examination of the spinal fluid revealed a decrease in sugar content, unchanged albumin level, and decrease in both hypertension of the fluid and the eosinophil count. After a 3-day course of corticotropin (ACTH) therapy (the total dose consisted of 60 units), a combined administration of prednisone (10 mg. a day) and isoniazid-aminosalicylic acid (17 Gm. a day) was instituted for a period of 16 days. Further improvement of symptoms was observed. However, hypertrichosis on the thighs and on the back, accompanied by loss of hair on the head, was noted. Arterial pressure increased to 145/95 mm. Hg. The level of urinary 17-ketosteroid, which at the beginning of the prednisone treatment was 7.5 mg. per 24 hours, increased to 14.5 mg. at the end of treatment. Edema, striae on the thighs, psychic alterations, and amenorrhea developed, the patient having received a total dose of 520 mg. of prednisone. Treatment with streptomycin and isoniazid was then reinstituted. Further improvement in the general condition, associated with regression of the side-effects to prednisone, followed. On the 100th hospital day the patient was able to leave bed for short periods of time. However, general deterioration occurred on the 110th hospital day, and despite the reinstituted antibiotic treatment the patient died 40 days later.

Cushing's Syndrome Caused by Bilateral Adrenocortical Hyperplasia. A. Giberti, B. Bonati, G. Virgillo and others. Minerva med. 49:733-742 (Feb. 28) 1958 (In Italian) [Turin, Italy].

The case of a 44-year-old woman with a colloid goiter and Cushing's syndrome caused by bilateral adrenocortical hyperplasia is reported. The patient was hospitalized because of 2 thyroid adenomas, with metastatic osteolytic lesions in the spinal column. Laboratory findings revealed elevated levels of free plasma 17-hydroxycorticosteroids, of not-conjugated urinary and total urinary titers of 17-hydroxycorticosteroids, of the urinary excretion of aldosterone, and of the total value of neutral 17-ketosteroids. The levels of hyperglycemia and glycosuria were those of steroid diabetes. The patient underwent 3 successive operations within 2½ months in the following order: bilateral resection of both thyroid lobes, total left adrenalectomy, and subtotal (nine-tenths of the gland) right adrenalectomy. Surgical therapy was effective, but it was necessary to supplement it with a subsequent maintenance therapy, consisting of prednisone in daily oral doses of 10 mg. combined with desoxycorticosterone given intramuscularly in a weekly dose of 10 mg. Blood pressure and glycemia returned to normal levels, urinary aldosterone disappeared, but renal sodium retention persisted. Clinical examination 7 months after the patient's discharge showed gain in weight, complete retrogression of hypertrichosis, disappearance of back pain, and restoration of menstruation and of libido.

Asymptomatic Gastric Retention in Diabetics (Gastroparesis Diabeticorum). P. Kassander. Ann. Int. Med. 48:797-812 (April) 1958 [Lancaster, Pa.].

Of 27 routinely admitted patients with diabetes mellitus, 9 had mild moderate diabetes and 18 had moderately severe diabetes. Of the 18, 6 men, between the ages of 35 and 47 years, had a patulous pylorus revealed on roentgenologic examination of the stomach. The roentgenograms also showed that the gastric contents could be expressed by hand, and even some peristalsis induced and observed, without changing the retention pattern. At 3 hours there was still 50 to 100% retention of the barium meal in the stomach, with the head of the meal in the ileum. At 6 hours there was 25 to 50% retention of the barium in the stomach, with the head of the meal in the ascending colon. Two of the 6 patients still had gastric retention of 15 to 30% after 24 hours. No abnormalities of the small intestine were observed. These findings seemed to indicate conclusively that these patients had a disturbance of propulsion—specifically, of expulsion—of stomach contents. The disturbance of motor function was attributed to the vagus nerve, and the roentgenograms were similar to those of gastric hypotonia after vagotomy. It appears then that a patient with diabetes at some point in the progression of his disease may "vagotomize" himself so far as the functional motor effectiveness of his stomach is concerned. The retention of stomach contents in a patient with diabetes mellitus may cause confusion so far as food intake and utilization are concerned.

Gastric retention in patients with diabetes mellitus was not known in the preinsulin era. This neuropathy resulting from the abnormal metabolism of unregulated diabetes appears to occur in patients whose diabetes has been known for from 3 to 12 years and to coincide with their use of long-acting insulin preparations. The probability that the metal zinc may be a causative factor presents itself. In the 6 patients the onset of gastric retention appeared to be insidious, masked, and without any definite symptoms. It occurs in diabetic patients with anorexia and diarrhea, with manifest neuropathy, as well as in those who have no symptoms other than their uncontrolled diabetes. The observed gastric hypotonia may adversely influence the satisfactory treatment of diabetes. The author's attempts at treatment were uniformly unsuccessful. Continuous or fractionated gastric suction, including lavage, as well as the 6-small-meal diet, in combination with administration of crystalline insulin alone, did more to improve diabetic control and alleviate the retention than did the use of drugs, including bethanechol (Urecholine) chloride or methacholine (Mecholyl) bromide. The effectiveness of vitamin supplements, including vitamin B_{12}, remained unclear in connection with the retention. The search for the syndrome of gastroparesis diabeticorum, which is more often overlooked than diagnosed, should be made as much a clinical routine as the search for other manifestations of diabetes mellitus.

Some Aspects of the Recent Epidemic of Influenza in Dundee. W. M. Jamieson, D. M. Green, J. M. Dunbar and others. Brit. M. J. 1:908-913 (April 19) 1958 [London].

During a recent epidemic of influenza, 263 male and 278 female patients were admitted to the King's Cross Infectious Diseases Hospital in Dundee, Scotland, between Oct. 1 and Nov. 15, 1957. They were studied by a combined group which included clinicians, epidemiologists, bacteriologists, and pathologists. The influenza was complicated by pneumonia in 262 patients (48%). Thirty-three of the 541 patients died. Most of the patients who died were 50 years of age or over, and many had preexisting cardiac or respiratory disease. Influenza virus A of the Asian type was isolated from pharyngeal washings obtained from selected patients. A fourfold rise in titer or a significant intial titer of complement-fixing antibodies to influenza virus A was found in the serums of 70 (91%) out of 77 patients examined. Staphylococci were the organisms most commonly isolated from the lungs of patients who had died in hospital. In 7 of 11 specimens the staphylococci were of the resistant type generally associated with hospitals. Second attacks of influenza occurred within a period of 7 weeks after the first attack in 6 patients. Encephalitis was observed in 1 patient with otherwise uncomplicated influenza and in 1 with influenza complicated by pneumonia.

In view of the fact that influenzal pneumonia was likely to be associated with a variety of organisms, and more especially in view of the possible occurrence of penicillin-resistant staphylococci, 231 of the 262 patients with influenza complicated by pneumonia were treated with chlortetracycline (Aureomycin) in doses of 1 Gm. daily for 5 to 7 days. A second course of antibiotic treatment was required by 33 patients who failed to respond satisfactorily to treatment with chlortetracycline; 29 of these were given erythromycin, and 4 were given novobiocin. Side-effects, such as diarrhea, were observed in 44 patients treated with chlortetracycline. A plea is made for further studies on the local epidemiology of influenzal pneumonia from the point of view of the bacterial component.

Etiology and Treatment of Ammonia Intoxication Associated with Disease of the Liver. J. S. Najarian and H. A. Harper. Surg. Gynec. & Obst. 106:577-585 (May) 1958 [Chicago].

The consistent occurrence of elevated levels of ammonia in the blood of patients with "hepatic coma" and the clearing of the sensorium that follows a reduction in the ammonia levels both indicate that ammonia intoxication is an important factor in the production of hepatic encephalopathies. The use of measures to combat ammonia intoxication is of great urgency, because neurological damage may be irreversible when the central nervous system is subjected to prolonged exposure to a high elevation of blood ammonia. The ammonia in the peripheral blood is derived largely from the gastrointestinal tract as a result of the action of bacteria within the colon on nitrogenous substrates, including blood which accumulates secondary to gastrointestinal hemorrhage. The treatment of ammonia intoxication is designed to reduce the amount of ammonia entering the portal circulation as well as to lower the level of ammonia in the systemic blood. The production of ammonia within the gastrointestinal tract in patients with severe disease of the liver can be controlled by (1) limitation of the intake of protein, (2) control of gastrointestinal bleeding, (3) prompt removal, by catharsis or lavage, of blood which may have accumulated from hemorrhage, and (4) oral administration of antibiotics to diminish the numbers and activity of the intestinal bacteria that produce ammonia from nitrogenous substrates.

The methods used to lower the level of blood ammonia are directed toward enhancing the reactions by which ammonia is normally metabolized in the body; these include amidation of glutamic acid or aspartic acid and the formation of urea, which is accelerated by arginine. Fifty patients were treated for ammonia intoxication originating from a variety of clinical situations, such as (1) exogenous ammonia intoxication, (2) portal cirrhosis associated with gastrointestinal hemorrhage, (3) surgical shunting procedures, or (4) acute hepatic insufficiency. For the immediate treatment of ammonia intoxication, the authors administered arginine hydrochloride intravenously. Each dose consisted of 500 cc. of a 5% solution of arginine in 10% dextrose administered over a 2-hour period. In the early phase of this study, a second dose was given after 4 hours, but later at least 8 to 12 hours were allowed to elapse before the second dose was given, because it was found that serum arginine levels remained high for 8 to 12 hours after the intravenous administration of 25 Gm. of the amino acid.

With the addition of arginine to other therapeutic measures used for ammonia intoxication, all except 2 of 50 patients initially improved, clinically and biochemically, even though 35 of them were first seen in deep coma. Only 14 (28%) of the patients died in this series; 9 of these had portal cirrhosis and bleeding esophageal varices.

Death From Asian Influenza, 1957: A Report by the Public Health Laboratory Service Based on Records from Hospital and Public Health Laboratories. Brit. M. J. 1:915-919 (April 19) 1958 [London].

Records of 477 patients who died of pneumonia during the 1957 epidemic of Asian influenza in Great Britain were obtained from public health laboratories in England, Wales, and Northern Ireland. Influenza virus A of the Asian type was isolated from the specimens of 195 (63%) of 310 patients tested. Of the 477 patients, 121 were children, 297 were adolescents and adults between the ages of 15 and 64 years, and 59 were patients over 65 years of age. Two hundred fifty-one were males and 226 were females. Twenty-five per cent of the deaths occurred in patients aged less than 45 years, who represented 60% of the total number. The most striking feature of the illness was the speed with which the patient's condition deteriorated and the rapid occurrence of death after admission to hospital. The duration of illness increased with age: 60% of children aged less than 5 years but only 10% of adults over 45 years of age died within 48 hours of onset. Pneumonia, often with hemorrhagic lesions of the lungs, tracheobronchitis, and lung abscess were the most frequent findings on autopsy.

The bacteriological diagnosis was in almost all the patients made from specimens obtained at autopsy. Staphylococcus pyogenes var. aureus was the commonest organism, being recorded in 288 (62%) of the 467 patients whose specimens were examined bacteriologically. Other pathogenic organisms were reported in 37 patients (7.9%), and the specimens of the remaining patients did not yield pathogenic organisms or were sterile. Staphylococci were found less frequently in young children (49%) and in elderly persons (31%); they were found most frequently in children of school age (88%). The fact that many of the patients in the youngest and oldest age groups yielded no pathogenic organisms suggests that at the extremes of life the virus infection can cause death without the assistance of bacterial infection. Antibiotic sensitivity tests on the staphylococci showed that about 65% of the patients who died within 48 hours of admission to hospital and of those who were never admitted had staphylococci sensitive to penicillin. Only 14% of the patients over 65 years of age had fully sensitive strains. These data suggest that most infections, except those in older patients, were acquired before admission to hospital.

Chronic Uremia Due to Polycystic Renal Disease Treated with the Artificial Kidney. S. Nakamoto and W. J. Kolff. A. M. A. Arch. Int. Med. 101:921-926 (May) 1958 [Chicago].

During the past 5 years (1952-1957), 13 patients with polycystic renal disease were seen by the artificial kidney team of the Cleveland Clinic Hospital. Eight patients were severely ill and were treated with dialysis. They received a total of 14 dialyses, in addition to the necessary medical management. Five patients were treated without dialysis. Seven of the 8 patients with severe uremia due to polycystic renal disease showed chemical and clinical improvement after dialysis and left the hospital much improved. Four of the 7 patients are still alive and are doing well from 3 months to 1 year after dialysis. Two of these have been able to return to their previous occupations, and 2 (61 and 69 years old) do not work but enjoy a reasonable amount of activity. Three patients died within 2 weeks to 2 months after discharge from the hospital. One patient died in the hospital from a far-advanced polycystic renal disease after 35 days of treatment, despite 3 dialyses. Four patients had recurrent hematuria that abated within 2 days; the 1 patient who died had continuous gross hematuria. Seven patients were able to keep a high-caloric diet after treatment. Protein was restricted to 50 Gm., but salt was allowed.

Most of the 8 patients probably were beyond recovery with medical management alone. In the others dialysis shortened the period of hospitalization. In serious cases more than 1 dialysis was necessary to consolidate the initial improvement. It sometimes took more than 14 days for renal function to recover. Hemorrhage from cysts needs not be a contraindication for dialysis. Surprisingly, after dialysis hypertension decreased an average of 30 mm. Hg systolic and 20 mm. Hg diastolic; and the blood pressure remained low for at least 3 weeks. Fortunate as this was, it is unexplained and needs conformation on a larger number of patients with polycystic renal disease and hypertension.

SURGERY

Lipomas of the Bronchus: A Presentation of Two Cases and an Analysis of the Literature. J. B. Hutcheson, W. M. Ashe and D. L. Paulson. J. Thoracic Surg. 35:638-642 (May) 1958 [St. Louis].

The authors report on 2 men, aged 56 and 32 years, respectively, with lipoma of the bronchus. They were admitted to hospital because of a nonproductive cough of 10 and 21 months' duration respectively. A chest roentgenogram obtained from the older patient revealed pneumonitis and atelectasis of the basilar segments of the lower lobe of the right lung. Bronchoscopy revealed a pulsating tumor which almost completely occluded the lumen of the basilar segmental bronchus. Thoracotomy revealed the basilar segments of the right lower lobe to be markedly involved in a suppurative pneumonitis, with thick vascular adhesions between the visceral and parietal pleura, and this lower lobe was resected. The pathological diagnosis was fibrolipoma of the right lower lobe bronchus with chronic obstructive pneumonitis. Follow-up of the patient during the next 16 months showed that he was free of symptoms. A chest roentgenogram obtained from the second patient revealed atelectasis of the upper lobe of the right lung. A biopsy obtained by bronchoscopy was suggestive of anaplastic carcinoma. A right pneumonectomy was performed. The pathological diagnosis was that of a polypoid lipoma of the right upper lobe bronchus with bronchiectasis of the upper lobe of the right lung and fibrosis and chronic pneumonitis of the upper, middle, and lower lobes. The patient had no further difficulties during the 12 years after his operation.

These 2 cases of bronchial lipoma brings to 20 the total number of cases reported in the literature in which surgery was performed. Five additional cases collected from the literature had been detected on autopsy. Lipomas as well as other benign bronchial neoplasms are capable of causing irreparable pulmonary parenchymal damage and on occasion may result in death of the patient. It is for these reasons that early diagnosis and surgical treatment are of great importance.

Preoperative Evaluation of Patients with Clinically Resectable Bronchogenic Carcinoma: Role of Biopsy of Nonpalpable Scalene Nodes. T. W. Shields and E. Shocket. A. M. A. Arch. Surg. 76:707-711 (May) 1958 [Chicago].

The authors report on 47 men, between the ages of 38 and 73 years, with clinically resectable carcinoma of the lung, who were admitted to the thoracic surgical service of the Veterans Administration Research Hospital and Passavant Memorial Hospital, Chicago, between May, 1954, and September, 1957. In an attempt to exclude by the preoperative evaluation of the patients those in whom a pulmonary resection would be of no benefit, biopsy of nonpalpable scalene nodes was performed, in addition to bronchoscopy and cytological examination of bronchoscopic aspiration material. Of the 47 scalene node biopsies, 32 were performed on the right side, 13 on the left side, and 2 were performed bilaterally. Despite the plan of bilateral biopsy for lesions of the lower lobe of the left lung, only 2 were carried out in the 6 patients with such lesions. Two patients had biopsy on the right side only and 2 on the left side. Lymph nodes were present in all specimens, and the number varied from 2 to 12, the average being approximately 5 nodes per specimen. Histological examination revealed metastatic tumor to be present in the nodes of 3 patients of the group. Two of these biopsies were on the right side; the other was on the left. Thus, the biopsy of nonpalpable scalene nodes revealed the presence of metastatic disease in 6.3%. Both the bronchial biopsy specimen and the cytological smear were positive in 2 of the patients with metastatic disease demonstrated in the scalene node biopsy; in the 3rd patient neither was positive.

The chest roentgenograms revealed a predominant hilar mass, with or without infiltration into the pulmonary parenchyma in 6 patients, bronchial obstruction with or without secondary infection in 23 patients, and peripheral pulmonary lesions in 18 patients. The 3 positive scalene node biopsies were obtained in patients with a prominent hilar mass on the roentgenograms of the chest; none were discovered in those with bronchial obstruction or with a peripheral lesion. Ten of the 47 patients who were originally thought clinically to have resectable lesions were not operated on. In 3 of these, metastatic carcinoma was found on the scalene node biopsy; 4 had extremely poor pulmonary function and heart failure with an associated old cerebral vascular accident; and 3 refused surgical intervention. Thirty-seven patients were explored surgically. In 13 patients (35.1%), the lesion was deemed nonresectable, owing to advanced local spread or extensive mediastinal node involvement. Twenty-four patients (64.9%) had a resection performed. The type of resection was dependent on the extent of the disease and the general condition of the patient. Fourteen pneumonectomies, 9 lobectomies, and 1 wedge resection were carried out.

The reported data suggest that biopsy of nonpalpable scalene nodes does not have a sufficiently high positive yield to justify its routine use in all clinically resectable cases of carcinoma of the lung. Its employment preoperatively is advised in those cases with a prominent hilar mass on the chest roentgenogram, or when the bronchoscopic biopsy tissue or the cytological smear reveals the presence of an undifferentiated-cell carcinoma.

Maximal Reconstitution of the Stenotic Mitral Valve by Neostrophingic Mobilization (Rehinging of the Septal Leaflet). C. P. Bailey and T. Hirose. J. Thoracic Surg. 35:559-583 (May) 1958 [St. Louis].

After a 9-year clinical experience with a large number of patients with mitral stenosis, subjected to mitral commissurotomy through the standard left-sided approach or by the right-sided method, the authors have devised a new and technically much superior type of mobilization of the mitral valve. It is based on the principle of converting the irretrievably destroyed flutter-valve action of the mitral valve to an efficient flap-valve mechanism. This effect is accomplished by a rehinging, or newhinging, of the septal cusp not only through its flexible midzonal tissue but also with respect to the usually shortened papillary suspension yoke which must be split longitudinally. Such a maximally corrective procedure has been described under the term "neostrophingic mobilization" of the valve. It cannot routinely be accomplished except with the technical advantage of the right-side approach.

Of 227 consecutive patients with essentially isolated mitral stenosis who were operated on according to this new method, digital mitral separation was used in 46 and instrumental mitral separation in 181. Complete satisfactory mobilization, with more than 90% of function reestablished, was accomplished in 156 patients (70%). Acceptable mobilization, with more than 70% of function reestablished, was obtained by 23 patients (10%). Results were unsatisfactory in 48 patients (20%); the valvular opening was limited in 24 of these patients, regurgitation was created or increased in 19, and subvalvular fusions was not completely relieved in 5. Calcification of the valve, which was considered severe in 34 patients, did not seriously reduce the surgeons' ability to achieve a satisfactory mobilization. Arterial embolization was produced at the surgical intervention in 7 patients (3%); it was cerebral in 5, and peripheral in 2. No limb amputations were required. Avoidance of the left auricular appendage as an entrance route would seem to have reduced the likelihood of thrombotic embolization. There were 4 operative deaths (2.5%) among the 156 patients in whom more than 90% valvular function was restored by the neostrophingic mobilization, and there were 7 operative deaths (10%) among the 71 patients who obtained a compromised technical result with less than 90% of valvular function being restored by the new technique. Among 1,000 patients subjected to mitral commissurotomy from the left side, there were 77 operative deaths (7.7%), and among 150 patients with mitral commissurotomy from the right side, there were 13 operative deaths (8.6%).

As shown by the persistence of auscultatory signs, most patients with mitral stenosis have received but partial and often temporary relief of their valvular obstruction when the older left-sided commissurotomy procedure has been carried out. Re-stenosis ultimately may be expected in a large proportion of these patients who have, in actuality, been subjected merely to linear (and limited) division of a fibrous stricture. It is believed that recurrence of mitral stenosis after complete neostrophingic mobilization will be rare, since the operation amounts actually to construction of a valve mechanism of different type, and since all the tissue cleavages extend well into normal unfibrosed structures. The reported data show that the early operative mortality and morbidity associated with complete reconstitution of the mitral valve are distinctly less than those associated with less complete operations. Because of certain unavoidable handicaps experienced during attempts to carry out an extensive mobilization of the valve structures with maintenance of full competence when the open technique is employed (by means of the pump-oxygenator), it is felt that a better and safer reconstitution of the stenotic mitral valve can be achieved by the closed method.

Granulomata of the Mediastinum Surgically Treated and Followed up to Nine Years. K. E. Karlson and J. J. Timmes. J. Thoracic Surg. 35:617-627 (May) 1958 [St. Louis].

The authors report on 17 men and 2 women, between the ages of 19 and 35 years, who were subjected to exploratory thoracotomy for mediastinal tumors, which proved to be granulomas of tuberculous or fungous origin. A mediastinal mass was discovered on routine roentgenologic examination in most of these patients. Two patients had some discomfort in the chest, 1 had pain in the right shoulder and right arm, 2 had slight daily rise of temperature for 3 weeks before admission to hospital, 4 patients complained of cough, and 1 had fever, malaise, and loss of weight. Physical examination was noncontributory in each patient. Hematological examination, urinalysis, and other usual laboratory examinations were not helpful in establishing the diagnosis. Eleven patients had a positive reaction to the skin test for tuberculosis, 4 had a positive reaction for histoplasmosis, but none had a positive reaction for coccidioidomycosis. Because of marked adherence of the mass to the trachea, bronchus, vena cava, or pulmonary artery in 6 patients, biopsy only was performed in 2 patients and partial excision of the mass in 4. In the remaining 13 patients the mass was removed completely. Pathological examination of the surgical specimens revealed that most of them were chronic fibrocaseous granulomas. Three of the lesions were positive for Mycobacterium tuberculosis on culture, and 1 was positive for acid-fast bacilli microscopically. One of the granulomas was positive for Histoplasma capsulatum. All the patients recovered from their thoracotomy without complications. After the operation 11 patients received combined treatment with streptomycin, isoniazid, and/or aminosalicylic acid (PAS) for periods ranging from 6 weeks to 1 year with no postoperative evidence of disease during follow-up periods. Active pulmonary tuberculosis subsequently occurred in 2 of 6 patients who did not receive postoperative chemotherapy with antituberculous agents.

Granulomas are generally assumed to develop as cystic caseous enlargements of lymph nodes, and 9 of the surgical specimens exhibited remnants of lymph nodes histologically. The remainder probably represent a complete destruction of the nodes. Exploratory thoracotomy is necessary for the diagnosis of a mediastinal granuloma when there is no other clinical evidence which would indicate the granulomatous nature of such a lesion. Removal of a portion of the granuloma for biopsy is essential in every case. Excision of as much of the mass as is feasible without undue risk is accompanied by no further complications than biopsy alone. Postoperative antituberculous therapy for 6 to 12 months should be administered to prevent subsequent spread of reactivation of tuberculosis unless a nontuberculous causation is definitely established.

A Study of 158 Cases of Esophageal Varices. L. G. Ludington. Surg. Gynec. & Obst. 106:519-526 (May) 1958 [Chicago].

This report is based on observations on 158 patients with esophageal varices seen at the Wadsworth Veterans Administration Hospital, Los Angeles, in the 3-year period from 1953 through 1955. All cases were substantiated by x-ray, endoscopy, autopsy, or evidence that bleeding could be controlled by esophageal tamponade. The main etiological factor in the development of esophageal varices is portal hypertension, caused by extrahepatic or intrahepatic portal bed block. The former usually results from portal vein thrombosis and generally occurs in children or young adults. The latter is thought to be due to obstruction of hepatic venules by obliterative fibrosis and distortion of cellular architecture. Cirrhosis, especially Laennec's cirrhosis, accounts for the great majority of the cases of bleeding esophageal varices. In this series, Laennec's cirrhosis accounted for 132 (or 83%) of the 158 cases of esophageal varices and an even greater percentage of those that bled. Excessive consumption of alcohol was established in 92% of these cases of Laennec's cirrhosis, and the average period of alcoholism before complications appeared was 17.3 years. One hundred eighteen (or 89%) of the 132 patients with Laennec's cirrhosis had esophageal hemorrhages, and 104 (or 88%) of these died within 1 year of the first hemorrhage. The average survival after the first hemorrhage was 6.4 months. The average number of hemorrhages per patient was 1.9. The average amount of blood given per hospital episode was 9 pt. Of those who bled and died, 20% died of exsanguination and shock; 59% died of exogenous hepatic coma secondary to hemorrhage; 14% died of a combination of shock and coma; and 7% died of miscellaneous causes (pneumonia, complications of emergency surgery). The average age at death was 51.6 years. Only 8 of 132 patients died of spontaneous coma without bleeding, and 6 of 132 patients had virgin varices (no bleeding while under observation).

Esophageal varices develop in up to two-thirds of all patients with hepatic cirrhosis, but not in all, and it has been suggested that the number and size of collateral channels might be a factor that determines whether varices develop. Patients with esophageal varices generally die of hemorrhage and its complications, and those in whom esophageal varices do not develop usually die of hepatic coma or intercurrent infections. Advances in treatment have reduced the number of deaths from intercurrent infections and have delayed death from hepatic coma, but these advances have given little help to patients with esophageal varices. Because of the toxic effects of blood absorbed from the gastrointestinal tract in cirrhotic patients, it is most important to stop bleeding as soon as possible. Balloon tamponade was used in 49% of the patients in this series; it caused bleeding to stop in 75% of these patients, but in 43% it recurred on removal of the balloon. This form of tamponade is only a temporary measure.

If liver function tests indicate adequate function to warrant surgical intervention, and if emergency ligation of esophageal varices is contemplated, it should be done as soon as replacement therapy has been completed, for repeated short trials of tamponade with recurrent bleeding only lead to further deterioration. Emergency ligation produced discouraging results in the cases cited in that only 1 of 7 patients survived. The portal-systemic vein shunt operations are generally accepted as the most effective method of lowering portal hypertension, decompressing the liver, and preventing future hemorrhage. In the series reviewed, 7 portacaval and 2 splenorenal shunts were done. These operations can be performed with a reasonable mortality of from 10 to 15% when the patients are properly prepared and selected. The basic liver damage remains, however, and the prognosis for future life depends on the extent of this liver damage and the strictness with which the patient adheres to the prescribed medical-dietary regimen. There has been no adequate comparable follow-up of cirrhotic patients treated medically to ascertain whether a shunt operation will prolong the life of such patients.

Finger-Fracture Method and Instrumental Commissurotomy in Mitral Stenosis: Analysis of 1,000 Patients. A. Actis-Dato, R. Gentille and Gin-Hua Chiu. Minerva med. 49:496-510 (Feb. 14) 1958 (In Italian) [Turin, Italy].

The authors discuss the correlation between the anatomicopathological condition of the mitral valve and the following 3 surgical techniques used in 1,000 patients who have undergone mitral commissurotomy since 1951: finger-fracture method, instrumental commissurotomy, and combined digital-instrumental method. This series of patients consisted of 331 men and 669 women, most of whom were 20 to 45 years of age. A slight degree of sclerosis with presence of few spots or complete absence of calcification but with preservation of valvular elasticity was observed in 627 patients (62.7%). The digital method was employed successfully in most of these patients. Sclerosis of the mitral valve with stiffened edges of the cusps but with unaltered valvular structure was present in 215 patients (21.5%). Heavy calcification of the mitral valve and deformed valvular structure were present in 158 patients (15.8%). Instrumental commissurotomy, alone or in combination with the digital method, was mostly used in the last 2 groups of patients. The use of a valvulotome has minimized the complications during operation. Tear of the myocardiac wall by the digital method was caused in 27 patients, and by instrumental commissurotomy in 2 patients only. Section of both commissures was made in about one-half of the patients. Insufficiency of the valve developed with approximately equal frequency and intensity after operation ascribed to either the finger-fracture method or instrumental commissurotomy. Instrumental commissurotomy was the technique of choice where commissures either were thickened by fibrosis and resistant to dilatation or were extensively calcified. Instrumental commissurotomy, alone or combined with the finger-fracture method, gave better results than the finger-fracture method alone with respect to the obtained extent of dilatation, functional correction of the valve, and smaller incidence of complications.

The Effect upon the Hypophysis of Radioactive Yttrium. W. A. Kelly, J. P. Evans, P. V. Harper and E. M. Humphreys. Surg. Gynec. & Obst. 106:600-604 (May) 1958 [Chicago].

The surgical removal of the hypophysis in 8 patients with advanced metastatic disease at various sites did not prove successful, and autopsies revealed fragments of residual pituitary tissue. Rasmussen and associates proposed destruction of the gland by the use of radioactive yttrium (Y^{90}) pellets, placed directly in the hypophysis. The new procedure was designed to lessen surgical time, to reduce morbidity and complications, and to produce more complete, if not total, destruction of the gland. Rough estimation of dosimetry by means of photographic film and extensive animal experimentation to determine the radiosensitivity of the hypophysis and parasellar structures preceded clinical use of Y^{90}. The authors present observations on 19 pituitary specimens radiated with varying quantities of isotopes with a wide spread of exposure time. The total millicurie dosages in this group varied from 1.3 to 6.5 mc., and the time intervals extended from 20 hours to 16 months.

At autopsy, the entire bony sella was removed en bloc and placed in formalin. If death occurred within 1 month after placement of the pellets, the specimen was set aside for radiation decay. The pituitary was then dissected out of the sella, and with the capsule kept in place, the beads were gently teased out of the gland, removal being necessary for the protection of the microtome blades. It was found that Y^{90} pellets, placed in the pituitary gland, effected total necrosis in a diameter of approximately 4 to 8 mm., depending on the activity of the pellet. Multiple pellet placement produced coalescent necrosis with a sharp border. A fibrous pseudocapsule formed in which a few pituitary cells became enmeshed. Tissue peripheral to the border showed chronic alteration, characterized by shrunken cells with small nuclei and clumped chromatin. The functional status of this tissue remains to be determined. In the 19 autopsy specimens from an operative series of 43 cases, none of the slides showed 100% destruction. It seems safe to assume that very few, if any, of the still living patients have 100% necrosis. Despite this fact, many of these patients have shown test evidence of reduced pituitary function. In 4 of the 43 patients there is good evidence of healing of metastatic lesions, and in 4 more of stabilized metastases. This finding might suggest that there is total arrest of pituitary function with viable, but altered, pituitary tissue; or beneficial clinical response may perhaps be seen in certain susceptible metastases when only a reduced pituitary function is achieved.

Section of the Sphincter of Oddi in Pathological Conditions of the Choledocho-Duodenal Junction. Y. Edlund and B. Jacobsson. Acta chir. scandinav. 114: 262-276 (No. 4) 1958 (In English) [Stockholm].

The authors report on 28 women and 8 men with anatomic changes and functional disorders of the choledochoduodenal junction who underwent cutting of the sphincter of Oddi in 2 hospitals in Sweden. Sphincterotomy as a primary operation was combined with cholecystectomy in 17 patients, 10 of whom had stones in the "ampulla" of Vater and 7 had stenosis of the choledochoduodenal junction. Sphincterotomy as a secondary operation was performed 1 to 19 years after an initial cholecystectomy in 19 patients because of attacks of pain alone in 10, pain combined with jaundice in 5, and pain combined with jaundice and pancreatitis in 4. Cutting of the sphincter of Oddi was performed transduodenally with an incision of about 10 mm.; a triangular portion of the anterior wall of the "ampulla" of Vater was removed. [The authors consider the term "ampulla" inappropriate, since the ampullary roentgenologic configuration, which has been observed in some patients, is the result of dynamic changes in muscular function and does not represent an anatomically preformed ampulla; in the absence of an anatomically more adequate term, "ampulla" is used with quotation marks.]

Excluding the group of 10 patients in whom stones obstructed the distal portion of the common bile duct, only 12 of the remaining 26 patients showed signs of functional disorder of the liver and/or pancreas. Pain alone was present in 14 patients. Sphincterotomy gave favorable results in 11 of 12 patients with pain combined with jaundice or pancreatitis; these 11 patients were free from sypmtoms on follow-up examinations 6 months to 2 years after the operation. Pain in the absence of signs of a pancreatic disorder persisted in only 1 patient who was a chronic alcoholic. Cutting of the sphincter of Oddi has seemed to be indicated in patients with persistent pain after cholecystectomy combined with signs of functional disorder of the liver or pancreas. Sphincterotomy gave poor results in the group of 14 patients in whom pain was the only symptom. Only 2 of 10 patients followed up for from 6 months to 4 years after the sphincterotomy were completely free from symptoms. This may have been brought about by the spasm of the intact portion of the sphincter complex being sufficiently marked to precipitate pain. Theoretically, it is possible that division of the entire sphincter complex in these patients may alleviate the pain.

Sphincterotomy did not lead to severe postoperative complications. Mild hyperdiastasuria was present for 1 or 2 days after the operation in 7 patients, all of whom had had signs of pancreatitis preoperatively, but it did not have any effect on the postoperative course. Microscopic examination of the resected portion of the "ampullary" wall showed changes in the form of infiltration of inflammatory cells, proliferation of connective tissue, and in some specimens muscular hypertrophy which possibly provides an organic basis for pain with or without functional disorder of the pancreas and/or liver.

Infection Following Splenectomy in Infants and Children: A Review of the Experience at Duke Hospital in Infants and Children During a Twenty-Two-Year Period (1933-1954). C. C. Huntley. A. M. A. J. Dis. Child. 95:477-480 (May) 1958 [Chicago].

There is at present considerable interest in the incidence of sepsis after splenectomy, particularly in infants. The author cites several recent reports on this problem and reviews the experience at Duke Hospital, Durham, N. C. Among 46 patients, 13 years of age and under, splenectomized at Duke Hospital during the years 1933 through 1954, there were 7 in whom severe infections developed after the operation. Five of these patients were under 1 year of age, and in 5 patients the basic disease was one which is associated with an increased susceptibility to infection. Three had the triad of eczema, purpura, and draining ears, 1 had portal hypertension, and 1 had Letterer-Siwe's disease (a form of xanthomatosis). Although, with this small series of cases, it is impossible to draw definite conclusions concerning the type of patient who will develop severe infections after splenectomy, one should be cautious in recommending splenectomy to patients with the eczema, thrombocytopenia, and otitis triad and to patients with diseases usually associated with an increased susceptibility to infection.

A Clinical Evaluation of Malignant Melanoma. W. R. Vogler, G. D. Perdue and S. A. Wilkins Jr. Surg. Gynec. & Obst. 106:586-594 (May) 1958 [Chicago].

The 254 malignant melanomas reviewed by the authors occurred in 253 patients who were observed over a period of 20 years. They accounted for 2.7% of the patients with cancer. Eight of the patients were of prepubertal age; 1 of these had 2 melanomas, 1 at the age of 5 and the other at the age of 11 years. The prepubertal lesions were treated by local excision and have caused no further trouble. These "juvenile melanomas" were excluded from any tabulations of end-results. The first line of defense in malignant melanomas is prevention. It is believed that the majority of these cancers originate in the junctional element of common nevi, particularly when located in uncommon areas as on the palms and soles, on the genitalia, and in those areas subjected to repeated trauma. The authors removed such nevi by surgical excision. The use of the electrodesiccation apparatus was avoided in the treatment of junctional and compound nevi because of the possibility of incorrect diagnosis or incomplete treatment. All lesions removed were submitted to microscopic examination. There has been no instance of malignant melanoma developing at the site of local excision of such a nevus or of metastasis occurring from a lesion adjudged benign at the time of removal.

Clinical suspicion that a mole is malignant is important in the management of malignant melanoma. Change in size or degree of homogeneity of pigmentation, cracking, weeping, or ulceration in a preexisting mole, or the appearance of a new one are all indications of possible malignant growth. Biopsy of such lesions is by complete excision, never by incision, since the latter practice may result in dissemination. Lesions known to be malignant melanomas are excised with a wide margin of normal skin down to and including underlying fascial structures with as little manipulation and traumatization of the tumor as possible. A case of apparent spontaneous remission is reported. The 5-and-10-year cure rates were 41 and 31% respectively. The prognosis was better for women. This held true when the sexes were matched as to stage of disease, size and location of lesions, and presence of ulceration. When the superficial melanomas were considered, the prognosis was equally good for both sexes, but when the tumor invaded the dermis, the prognosis again was better for women. Lesions not metastasized to regional lymph nodes had a better prognosis. The authors found that ulceration, and particularly ulceration in small lesions, indicates a poor prognosis. Superficial melanomas, although the prognosis is better, are potentially as dangerous as invasive lesions and should be treated as fully malignant melanomas. Tumors arising on the trunk involve a poorer prognosis than lesions about the head or the extremities. Early, forthright, and consistent treatment of melanoma is surprisingly efficacious. The value of prophylactic node dissection of the appropriate lymphatics, while theoretically probable and inferred by accumulating evidence, does remain to be proved. A more hopeful outlook regarding melanoma is justified.

NEUROLOGY & PSYCHIATRY

Acute Encephalopathy Due to Water Intoxication. A. G. Swanson and O. A. Iseri. New England J. Med. 258:831-834 (April 24) 1958 [Boston].

While it is generally considered that healthy persons can drink large quantities of water without ill-effect, this communication reports 2 cases of acute delirium and convulsions that followed the voluntary ingestion of massive volumes of water. The first patient had taken large quantities of beer on 2 successive days, then he had taken very little food and drink for 4 days, but 6 hours before admission he complained of unquenchable thirst and consumed "glass after glass" of water until he had a convulsion. It was estimated that his water intake was in excess of 1 gal. No abnormalities were found on examination of the optic fundi, pharynx, chest, heart, or abdomen. Neurological examination revealed an abnormal sensorium, vigorous power in all extremities, absent tendon reflexes in the arms, hyperactive stretch reflexes in the legs, and bilateral ankle clonus. The plantar reflexes were extensor bilaterally. The temperature was 99.4 F (37.5 C) by rectum; the pulse, 100, and the respirations, 28. The blood pressure was 300/160 mm. Hg. A lumbar puncture showed an initial cerebrospinal-fluid pressure equivalent to 230 mm. of water that fell to 120 mm. after removal of 8 ml. of fluid. Therapy was started with intravenous infusions of hypertonic (5%) sodium chloride solution. During the first hour the patient had 2 more generalized convulsions, which were controlled with intravenous administration of amobarbital sodium. He gradually became oriented. He had no recollection of the preceding 48 hours. There was a mild left-sided hemiparesis that persisted until the 3rd hospital day; the patient was discharged clinically well on the 6th hospital day.

The second patient, a 52-year-old man, had taken hot water at a rate of approximately 1 glass every 5 minutes to induce defecation, but at the end of 2 hours he was still unable to defecate, so he took 2 tap-water enemas. Each enema was in excess of "1 pt." in volume. Both were held briefly and then expelled. His only recollection of sensations after the enemas was of heavy breathing and lightheadedness. He was admitted to the psychiatric ward because of the sudden onset of irrational and agitated behavior. He was unable to give a history. He had projectile vomiting and was incontinent of feces and urine. Skin turgor was normal, as were the optic fundi, heart, lungs, and abdomen. Neurological examination showed an abnormal sensorium, symmetrically hyperactive stretch reflexes, bilateral patellar and ankle clonus, and bilateral Babinski signs. A lumbar puncture, performed with difficulty because of the patient's struggling, showed an initial cerebrospinal-fluid pressure equivalent to 400 mm. of water. This patient was discharged clinically well 2 days later. Water intoxication can occur in normal persons when the rate of intake of a large volume of water temporarily exceeds the ability to maintain the isontonicity of body fluids through prompt diuresis. Delayed diuresis may be caused by prior electrolyte depletion or by the rapid absorption of water from multiple sites. The cause of increased neuroexcitability produced by rapid changes in serum tonicity is not known. Other studies, however, have shown that sudden hyponatremia induces intracellular hypernatremia and an increased neuroexcitability.

Cerebral Abscess: Etiology, Diagnosis, Therapy and Prognosis Illuminated by 114 Cases. C. V. M. Fog. Nord. med. 59:487-491 (April 4) 1958 (In Danish) [Stockholm].

The material consists of 114 cases of cerebral abscess, in 89 men and 25 women, from the neurological departments of the Rigs Hospital and the Bispebjerg Hospital, Copenhagen, from 1935 to 1956. There were 55 deaths. The most frequent causes of brain abscess were infections originating from the ear or nose; next in frequency were infections from the lungs. Thirty-nine abscesses were otorhinogenic; 28 were thoracogenic. The mortality was highest in the thoracogenic cases, where the patients were often in poor condition due to their pulmonary disease and the abscesses were not infrequently multiple. The prognosis was best in the cases with sterile abscesses and most unfavorable in the cases with streptococci. Staphylococcus aureus was the bacillus most often found on cultivation, and the mortality was about 50% in this group. Diagnosis may be difficult. Brain abscesses may be present without demonstrable leukocytosis or choked disk. The intracranial pressure, measured in 91 cases, showed normal values in over one-third of the cases. In half of the infratentorial cases the values were normal. Most of the cases were supratentorial. Localization to the brain stem was seen in only 2 cases. A follow-up revealed that 6 of the 59 survivors died of other causes, and 4 no longer lived in Denmark. Of the remaining 49, the ability to work was reduced in not quite half of those with supratentorial abscesses, slightly less than one-third of whom had epilepsy, while 8 of the 9 survivors of infratentorial abscesses were well. Most patients were treated by excision. The mortality does not seem to be higher with this method of treatment than with more conservative methods. Total excision seems to be the best method of treatment in patients with multiple abscesses. Antibiotic treatment according to modern lines has improved the prognosis for patients with brain abcess.

GYNECOLOGY & OBSTETRICS

The Relative Frequency of Various Anatomic Sites as the Point of First Metastasis in 32 Cases of Chorionepithelioma. H. Acosta-Sison. Am. J. Obst. & Gynec. 75:1149-1152 (May) 1958 [St. Louis].

This study was made to determine the point of first metastasis in 32 patients with microscopically diagnosed chorionepithelioma, who were observed at the Philippine General Hospital, Manila, during the 6-year period from 1950 through 1955. The primary site of metastasis was in the lungs in 14 of the 32 patients (43.75%) and in the vagina in 10 of the patients (31.21%). The lungs were eventually involved in 94%, and the vagina in 43.75% of the 32 patients. Other organs frequently affected were the brain, liver, kidneys, and ovaries. Less common secondary points of involvement were the intestines, stomach, spleen, adrenals, parametrium, mesentery, Douglas' cul-de-sac, and the lateral pelvic wall. The mortality rate in all the sites of primary metastasis, except the broad ligament, the vagina, and the lungs, was 100%. Death occurred in 1 of the 3 patients with metastasis to the broad ligament—a mortality of 33.3%, in 10 of the 14 patients with vaginal metastases (71.42%), and in 24 of the 30 patients with metastases of the lungs (80%). Metastases in the lung or the vagina, in both the vagina and the lung, or in the broad ligament are not necessarily fatal; if they are recognized and treated early, recovery may follow. Six of the patients with primary metastases in the lung or in the vagina recovered because they were treated early. However, advanced metastases in these regions, whether they spread to other organs or not, are invariably fatal.

Biological Sex Differences with Special Reference to Disease, Resistance and Longevity. L. B. Shettles. J. Obst. & Gynaec. Brit. Emp. 65:288-295 (April) 1958 [London].

The author comments on various biological differences between the human sexes. In every population fewer females are conceived. Why more males than females are conceived is not known, but the Y chromosome is smaller than the X. Consequently the Y-containing spermatozoon is lighter and may well have a smaller head. The smaller head could permit more rapid migration to and penetration of the ovum. With the difference in size of the sex chromosomes, the total gene content is not the same in the 2 sexes. This difference in total number of genes most likely is reflected in the different biological aspects of males and females. Possibly the female with XX chromosomes carries factors for longevity not present in XY chromosomes of the male. In utero and in every age group throughout life, more males succumb. Females are more resistant to disease, the stress and strain of life. They are better operative risks, have fewer postoperative complications, and continue to outlive males. In general, their biological existence is more efficient than that of males.

The greater resistance of the female sex is exemplified by a longer life. The shorter life span of males is characteristic throughout the animal world. In 42 species, including invertebrates, vertebrates, and mammals, the females outlive the males. This should be kept in mind when differences in modes of life and habits are cited as factors resulting in difference in longevity in man and woman. It has been concluded that the same type of curve encountered everywhere for the increased death rate of men in the higher age groups is indicative of an inferior power of resistance, instead of special conditions regarding the population. The possibility that woman's reliable supply of gamma globulin, the blood fraction that contains antibodies against infectious diseases, is related to the fact that women live longer than men has been considered. Endocrine and glandular changes in a woman normally are perfectly synchronized with her meeting stress in one of her most important roles in life, bearing offspring. In utero, 20 to 30% more males than females die. Also, during the first years of life more males succumb than females. Accordingly the explanation for the over-all higher male mortality is not to be found in exertion, the often dangerous work of men, or the abuse of alcohol and tobacco.

Hydatidiform Mole: A Clinical and Pathological Study of 72 Cases, With Reference to Their Malignant Tendencies. B. J. Logan and L. Motyloff. Am. J. Obst. & Gynec. 75:1134-1148 (May) 1958 [St. Louis].

The authors report on 72 patients with hydatidiform moles, consecutively admitted and treated from 1929 to 1955 at the Woman's Hospital, Division of St. Luke's Hospital, New York. Special reference is made to 8 patients in whom chorionepithelioma later developed. The age of the patients ranged from 19 to 48 years. Curettage was performed on 64 of the 72 patients. Histologically, these 64 patients were classified in 3 groups. The first group consisted of 31 patients, in whom the moles showed no histological evidence of trophoblastic proliferation or invasion; yet in 1 patient malignant manifestations (choriocarcinoma) developed 5 weeks later. In 2 of the 14 patients of the second or intermediate group, with minimal or localized trophoblastic proliferation, a diagnosis of chorioadenoma was made 1 month and 4 months, respectively, after curettage. There were 19 patients in the third group, with histologically demonstrated excessive trophoblastic proliferation, associated with infiltrative tendencies, but in only 5 of these patients (26%) was histological proof of malignancy obtained. Periodic quantitative determinations of chorionic hormone—the Aschheim-Zondek test—proved to be the most sensitive and accurate indicator in detecting entopic or ectopic chorionepithelioma. Negative histological findings, in the presence of positive titers of chorionic hormone, indicate that the chorionic elements may be lodged deep in the myometrium beyond the reach of the curette or may have metastasized to distant organs, such as the lungs.

Three patients showed negative findings on curettage, but the roentgenograms revealed shadows in the lungs, which were interpreted as metastatic lesions. These cases illustrate the limitations of curettage as a diagnostic procedure and show the importance of making repeated quantitative determinations of chorionic hormone. Eight of the 72 patients (11%) presented a persistently positive or rising titer of chorionic hormone after removal of the mole, and as a result the diagnostic curettage was repeated and roentgenograms were made of the chest in these patients. The final diagnosis in these 8 patients proved to be chorioadenoma destruens in 5, chorioadenoma in 1, and metastatic moles in the lungs in 2. Positive radiologic findings in the presence of negative histological findings should be considered inconclusive evidence of malignant metastases, unless substantiated by positive titers of chorionic hormone. In this study no true correlation was found between the histological pattern of the mole and its malignant tendency. There were no deaths or recurrences in this series.

Long-Range Studies of the Biologic Behavior of the Human Uterine Cervix: III. Squamous Metaplasia. R. R. de Alvarez, D. C. Figge, D. V. Brown and K. J. May. Am. J. Obst. & Gynec. 75:945-956 (May) 1958 [St. Louis].

Recent concern with the early diagnosis of cancer and recognition of the importance of in situ changes have led to renewed interest in the significance of squamous metaplasia in the epithelium of the uterine cervix. The present report was designed to clarify some of the assumptions often associated with this epithelial alteration. By studying sequential biopsy material, the authors believed it would be possible to determine (1) the prevalence of squamous metaplasia in presumably healthy women, (2) the importance of a wide variety of possible causative factors, and (3) the implications of squamous metaplasia with particular reference to its role as a precursor of cancer of the cervix. A group of 954 presumably healthy asymptomatic women was followed for over 5 years. Initially, a careful history was taken, and a physical examination was made of each subject. These have been followed by periodic pelvic examinations, study of the vaginal cytology, and biopsies of the cervix. The youngest subject was 14 years of age, and the oldest was 83.

In the 10-to-19-year age group, 57.2% of 28 patients were found to have metaplasia, while in the 20-to-29-year age group the incidence was 68.2% of 88 patients. After the third decade, the prevalence dropped gradually until, in the 60-to-69-year age group, only 40.7% of 27 patients presented metaplasia. The data on age distribution appear to be highly significant. Statistical analysis of grouped age brackets, however, shows that the significance of age in relation to the occurrence of metaplasia applies only to patients aged less than 40 years. The occurrence of pregnancy exerted no influence on the prevalence of metaplasia, nor could a relationship be demonstrated between cervical metaplasia and race, marital status, menarche, time of menopause, type of menopause (physiological or surgical), leukorrhea, bloody discharge, history of venereal disease, use of contraceptives, circumcision of husband, height, weight, body type, size of breasts, presence of enlarged inguinal nodes, gravidity, parity, clinical parity of the cervix, type of cervical mucosa, size or irregularity of the uterus, or adnexal or rectal pathology. The presence of cervical eversion in women under 40 years of age, however, is associated with a significantly increased prevalence of metaplasia. Because of the low incidence of cervical malignancy in the general population and the comparatively small group of such patients studied, no direct evidence has yet been obtained concerning the relationship between cervical metaplasia and cervical malignancy.

PEDIATRICS

Three Cases of Myocarditis in Children Less Than One Year of Age. C. M. McCue. Pediatrics 21:710-718 (May) 1958 [Springfield, Ill.].

The author reports on 2 boys and 1 girl with myocarditis in whom the diagnosis was made when they were less than 1 year old. The infants showed cardiac enlargement, absence of significant murmurs, marked electrocardiographic abnormalities, particularly of the T waves and S-T segments, and essentially normal blood pressure. In contrast to the evidence of cardiac failure in previously reported cases of myocarditis in children, none of the

3 patients was recognized as severely ill when first examined. In the first boy electrocardiograms and roentgenograms of the chest would probably not have been made if epileptic attacks had not occurred. The severity of the electrocardiographic changes at that time suggested fibroelastosis. The course of the disease, with improvement in the electrocardiographic changes but recurrent abnormal electrocardiographic findings on 2 occasions, supported the diagnosis of myocarditis. Two attacks of acute cardiac failure accompanied acute respiratory infections; yet the patient improved dramatically after these attacks, even without the administration of digitalis, when treated with antibiotics and oxygen. The electrocardiograms improved further and the size of the heart decreased in this boy when he later received digitalis. The girl had marked cardiac enlargement and tachycardia with rapid respirations, but frank cardiac failure did not occur; it apparently was averted by the prompt use of digitalis. The excellent response to this drug and to antibiotics over the last year has been most gratifying. The entirely normal electrocardiogram at the time of writing and the excellent clinical course have made discontinuation of digitalis therapy possible, and the patient has continued to be asymptomatic for several months since cessation of such therapy.

The second boy was first recognized to have a large heart and rapid pulse and respiratory rates at the age of 9 months, but the diagnosis of myocarditis was not suspected until cardiac failure occurred suddenly 1 month later, with rapid progression to death within a few hours. There was no time for digitalis to be effective in this patient. Autopsy revealed that the left ventricle was markedly dilated and hypertrophied with flattened, densely scarred endocardium. The right ventricle was slightly hypertrophied and the right ventricular cavity was encroached upon by the hypertrophied dilated interventricular septum. There were focal areas of lymphocytic infiltration in the myocardium, endocardial fibrosis of the left ventricle, and vacuolation of muscle fibers in the subendocardial layer of the left ventricle.

Although myocarditis is not frequently observed in children less than 1 year old, its presence must be suspected in those with the findings mentioned. Appropriate therapy should be instituted promptly, including administration of digitalis, adequate treatment with antibiotics to control any immedate infections, and moderate restriction of activity for a brief period. Because infections have precipitated cardiac failure in some patients, it would seem desirable to administer antibiotics for at least 1 year. In the 2 patients who survived, the size of the heart decreased during periods of 12 and 18 months, respectively, although it has not yet returned to normal.

Hypersensitivity **Reactions Associated With Sodium Para-Aminosalicylate Therapy: Four Case Reports and Review of the Literature.** N. Matsaniotis, J. Jacobs and M. H. D. Smith. Pediatrics 21:781-792 (May) 1958 [Springfield, Ill.].

The authors report the occurrence of a hypersensitivity reaction to aminosalicylic acid (PAS) in 3 of 100 children with various forms of tuberculosis who were treated at Bellevue Hospital, New York, with antimicrobial agents, including aminosalicylic acid and its derivatives. There were 2 girls, aged 4 and 7 years, and a 5-year-old boy. A similar hypersensitivity reaction to aminosalicylic acid was observed in a 4th patient, a 2½-year-old girl. The manifestations of acquired hypersensitivity to aminosalicylic acid consisted of fever and a papulomacular rash in all 4 patients; these were accompanied by headache, chills, malaise, anorexia, and conjunctivitis in several patients and by generalized lymphadenopathy in 1. Eosinophilia was observed in 1 patient, absolute leukocytosis in another, and considerable monocytosis in still another. Granulocytopenia occurred in the 7-year-old girl 23 days after treatment with aminosalicylic acid was started; administration of all drugs except that of penicillin was stopped, and the patient recovered rapidly. Jaundice occurred in the 4-year-old girl 1 month after treatment with aminosalicylic acid was started and 12 days after the first occurrence of fever. Desensitization to the drug, which is a safe, and nearly always successful procedure, was achieved in 3 patients.

Today, when many tuberculous children are treated in their homes, it is sound medical practice to warn the parents to stop giving aminosalicylic acid at the onset of fever, or any unusual symptom occurring within 2 months of starting treatment, and to report immediately to their physician. From the diagnostic point of view, any rise of temperature occurring between the 2nd and the 6th week of therapy should be regarded as a hypersensitivity reaction until proved otherwise. As soon as the diagnosis of hypersensitivity is suspected, the administration of the drug should be discontinued. It has been common experience that the more severe reactions occurred when administration of aminosalicylic acid was continued in the presence of symptoms of hypersensitivity. It is difficult to know whether to continue the administration of other antibiotics in the presence of a hypersensitivity reaction to aminosalicylic acid. Probably this should be avoided in most patients during the acute phase of the reaction, lest hypersensitivity develop to these drugs. Desensitization should be attempted unless specific contraindication exists. Since jaundice may occur as long as 3 weeks after the initial manifestation of hypersensitivity, it would seem wise not to undertake this procedure sooner.

OPHTHALMOLOGY

Ocular Lesions of Temporal Arteritis. H. P. Wagener and R. W. Hollenhorst. Am. J. Ophth. 45:617-630 (May) 1958 [Chicago].

Fifty-four of 122 patients, 64 women and 58 men between the ages of 60 and 83 years, with temporal arteritis, who were observed at the Mayo Clinic up to the end of 1956, had some degree of impairment of vision due to their disease. Fifteen were blind in both eyes; 18 were blind in 1 eye. The most common local cause of the loss of vision was acute ischemia of the optic nerve (ischemic optic neuritis), which was present in 64 eyes; in 5 of them it was of the retrobulbar type, i. e., without visible edema of the disk, while edema of the disk was visible ophthalmoscopically in the remaining 59 eyes. Occlusion of the central artery of the retina was observed in 2 eyes and occlusion of both the central artery and the central vein in 1 eye. Ischemic retinopathy without complete infarction of the retina was noted in 4 eyes, and residuals of previous acute lesions of the optic nerve or retina in 24 eyes. Rotations of 5 eyes were limited as the result of paresis of ocular muscles. Suspicion that the ocular lesions are a part of the syndrome of temporal arteritis may be heightened if the patient gives a history of general malaise, weakness, anorexia, and loss of weight; 27 patients complained of these symptoms. The diagnosis of temporal arteritis was confirmed by biopsy of a temporal artery in 72 of the 122 patients. Since October, 1949, most of the patients with temporal arteritis, with or without ocular involvement, seen at the Mayo Clinic have been treated with cortisone or related adrenal corticosteroids. There has appeared to be little difference in the rate of objective healing of an ischemic optic neuritis with or without steroid therapy, but steroid therapy seemed to improve the visual results in patients in whom there was only partial loss of vision at the time treatment was started.

Permanent loss of vision is preceded at times by attacks of brief, transient loss. The anatomic basis of the lesions of the optic nerve, the retina, and the ocular muscles is giant-cell arteritis involving the ophthalmic artery or its branches. The histological lesions of temporal arteritis are distinct from those of periarteritis nodosa, but there may be some, as yet undetermined, relation between these 2 entities. The history given by the patient and the evidence obtained by palpation of the temporal and occipital arteries and by determination of the erythrocyte sedimentation rate are adequate to establish the diagnosis with a sufficient degree of accuracy in most of the patients coming to the ophthalmologist with eye lesions suggestive of temporal arteritis. To avoid errors in diagnosis, histological studies of segments of the apparently involved arteries removed at biopsy should be obtained whenever possible, particularly from patients with atypical findings. It is possible that early diagnosis of temporal arteritis and prompt and adequate treatment with adrenal corticosteroid will reduce the incidence of blindness which is the most distressing sequel of this disease.

Giant Cell Arteritis as Cause of Acute Blindness. R. Seitz. Klin. Monatsbl. Augenh. 132:383-403 (No. 3) 1958 (In German) [Stuttgart, Germany].

The author applies the term "giant-cell arteritis" to the entity which in the American literature is generally referred to as "temporal arteritis." At the eye clinic of the University of Tübingen 7 patients in whom temporal arteritis resulted in acute blindness were observed in the course of 18 months. The author believes that in Germany temporal arteritis has not received the attention it deserves as a cause of acute blindness, and since, according to American reports, the eyes become involved in only up to about 50% of the cases, a certain percentage of cases of temporal arteritis will remain unrecognized. The disorder can be definitely identified only on the basis of histological studies; on the basis of localization of the pathological infiltration of the vascular wall, the author classifies giant-cell, or temporal, arteritis as an angiitis.

While the changes are found chiefly in the media, the adventitia and the intima are also involved. Whereas in the adventitia the infiltrations are mostly inflammatory, the intima shows proliferations of the granulation tissues from the media, or there is new formation of the intimal tissue. Thus, the picture is one of panarteritis. Occlusion is produced in the larger arteries by filling tissues, in the smaller arteries by hyperplasia of the intima. In 1 patient the artery had been completely transformed into granulation tissue. The author feels that acute blindness resulting from temporal arteritis is frequently mistaken for blindness from closure of the central retinal artery. He lists differentiating signs of these 2 conditions but also points out that, according to some investigators, giant-cell arteritis may eventually cause closure of the retinal arteries by embolization of granulomatous tissue. With regard to the treatment of temporal arteries, the author says that in 3 of his patients the considerably diminished function was favorably influenced by cortisone, antibiotics, and vasodilators. In 1 patient the visual fields and acuity improved under this therapy from practically blindness in both eyes to 1.0 and 0.6. At the same time dynamometric studies showed that the initially almost arrested circulation in the peripheral intracranial vessels became almost normal This suggests that the treatment of temporal arteritis is quite promising.

Therapeutic Application of a New Water-Soluble Preparation of Prednisolone, Administered Intrathecally for Tuberculous Meningitis. J. Santopadre. Minerva med. 49:615-617 (Feb. 21) 1958 (In Italian) [Turin, Italy].

The author made a comparative study of the therapeutic effect of hydrocortisone and of an Italian preparation of water-soluble prednisolone, both being administered intrathecally to 2 groups of patients with tuberculous meningitis. Tolerance to prednisolone was tested in 16 adults with tuberculous meningitis in whom the spinal fluid had returned to normal. No chemical or cytological change in the spinal fluid of these patients was observed. There was no subjective intolerance to the drug.

Hydrocortisone therapy was given to a group of 24 patients and prednisolone therapy to a group of 12. Patients in both groups also received 2 courses of prednisolone therapy given orally; each course lasted about 3 weeks. Water-soluble prednisolone was more efficacious than hydrocortisone (both of which were administered intrathecally) for the treatment of tuberculous meningitis in this series of patients. Even small doses of prednisolone (1 to 3 mg.), which were equivalent to one-third of the hydrocortisone doses, have produced a therapeutic effect. Prednisolone therapy brought about normalization of the spinal fluid in half the time that was required for hydrocortisone therapy. Albumin found in the spinal fluid was the component which responded best to prednisolone therapy. The patients tolerated the prednisolone therapy well. There was no incidence of superinfection in this series of patients.

Investigations of the Antirheumatic Action and the Tolerance of Intra-articular Injections of a Water-Soluble Preparation of Prednisolone. R. Capra and R. D'Oria. Minerva med. 49:690-693 (Feb. 24) 1958 (In Italian) [Turin, Italy].

An Italian preparation of water-soluble prednisolone was given to 30 hospitalized patients, 18 of whom had rheumatoid arthritis, 2 gouty arthritis, 3 a chronic ankylotic periarthritis of the shoulder, and 5 arthrosis. The patients received 68 injections in 37 joints; 49 injections were given in the knee, 2 in the wrist, 12 in the shoulder, 3 in the hip, and 2 in the tibiotarsal joint. Most of the patients received 2 or 3 injections in doses varying between 5 and 10 mg., with a period of 48 hours to 10 days in between.

All the patients derived benefit from the therapy except 1 with rheumatoid arthritis and 1 with chronic ankylotic periarthritis of the shoulder. Improvement lasted up to 5 days in 21 joints and between 5 and 13 days in 14 joints. A dose of 10 mg. was more effective than a dose of 5 mg. Some patients complained of an acute local pain promptly after receiving the injection. Pain was temporary and lasted a few minutes to 1 hour; it did not cause deterioration in the clinical picture, and it was probably caused by the solvent rather than by the drug. The opinion of the authors is that intra-articularly administered water-soluble prednisolone has an antirheumatic effect 2 or 3 times greater than the same amount of hydrocortisone acetate. Water-soluble prednisolone also has the advantage of making it possible to administer the drug simultaneously by the intravenous route and by the intra-articular route when such procedure is indicated.

Intra-Arterial Nitrogen Mustard in the Treatment of Pelvic Cancer. *I. H. Krakoff and R. D. Sullivan.* Ann. Int. Med. 48:839-850 (April) 1958 [Lancaster, Pa.].

Intra-arterial administration of nitrogen mustard was practiced in 29 patients, between the ages of 20 and 84 years, with pelvic cancer. Six had carcinoma of the uterine cervix, 7 had carcinoma of the ovary, 5 had neoplasm of the uterus and the fallopian tubes, 4 had carcinoma of the rectum, 4 had lymphoma, and 3 had miscellaneous neoplasms. Most of the patients were given a single dose of 0.4 mg. of nitrogen mustard per kilogram of body weight. It was administered with a thin-walled needle being introduced directly into the femoral artery. An appropriate polyethylene catheter was then threaded through the needle and passed retrograde through the femoral artery into the abdominal aorta at a level which was calculated to be 2 or 3 cm. above the bifurcation. In the first few such procedures the catheter was localized by a roentgenogram. This has not been necessary routinely, however, since introduction of the catheter to a distance of 25 cm. from the skin puncture has proved satisfactory in the average case.

The procedure described for the intra-arterial administration of nitrogen mustard is simple and has caused no discomfort beyond the transient nausea and vomiting usually associated with the systemic administration of nitrogen mustard. No serious technical or toxic complication was observed. Some degree of improvement was obtained by 18 patients (62%). There was no improvement in 11 patients (38%). The therapeutic response, when it occurred, varied from 3 weeks to 6 months in duration. Treatment in 12 patients with the subjective symptom of pain was followed by improvement in 9. In 21 of 29 patients with objective signs, a positive response to treatment occurred, such as measurable decrease in the size of a tumor mass and increase in urinary flow. The best results were seen in the patients with lymphomas and carcinomas of the ovary and the uterus. Patients with carcinoma of the uterine cervix responded less well, and those with carcinoma of the rectum were therapeutic failures. Intra-arterial administration of nitrogen mustard is a useful procedure in the palliative care of patients with pelvic neoplasms of ovarian, uterine, or lymphomatous origin.

Psychotic Reactions Due to Anti-tuberculous Drugs. E. H. Hare. Tubercle 39:90-95 (April) 1958 [London].

Of the various drugs which have been introduced during the past 15 years for the treatment of tuberculosis, 3 have been suspected of occasionally causing florid psychotic reactions. These are streptomycin, iproniazid, and isoniazid. The author presents the histories of 4 patients in whom mental disorders developed while they were being treated with antituberculous drugs. The mental disturbances were of such severity as to necessitate removal of the patients to a mental hospital. Streptomycin had been given to 2 of these patients, and both recovered soon after the drug was withdrawn. The other 2 cases were associated with isoniazid therapy, and in both patients the mental disturbances persisted for many months. Arguments are advanced to support the probability that isoniazid and streptomycin may be the precipitating causes of serious psychosis. Because psychosis associated with isoniazid may be prolonged, manifest mental changes in patients on isoniazid therapy should, in general, be an indication for withdrawing the drug.

PATHOLOGY

Serological Studies with Asian Strain of Influenza A. S. K. R. Clarke, R. B. Heath, R. N. P. Sutton and C. H. Stuart-Harris. Lancet 1:814-818 (April 19) 1958 [London].

When the virus of Asian influenza was isolated in Singapore in May, 1957, it was found to be an influenza A strain because it contained the soluble complement-fixing antigen common to all influenza A strains. It differed from all previous influenza A strains, however, in that the hemagglutination-inhibition test, which detects strain-specific antigens, showed no cross reactions with any previous strain. This explains the finding that only a very small proportion of people before exposure to the virus had hemagglutination-inhibiting antibodies against the Asian strain. This absence of antibodies in the preepidemic serums gave an opportunity for studying the effect of the epidemic of Asian influenza on the serologic status of the population. Studies were made by hemagglutination tests on random serums collected before the outbreak between 1955 and 1957, some of which were pooled by age group, and on individual and other pooled serums collected in November, 1957, 2 months after the peak of the epidemic. Serums from patients with influenza in 1949, 1951, and 1956 and from persons inoculated with various influenza-virus vaccines in 1955 and 1956 were also tested by the same methods in the hope of throwing light on the relationship between the Asian influenza virus antigen and those appropriate to earlier influenza A viruses.

Hemagglutination-inhibiting antibody to the Asian influenza virus antigen was detected in 70% and complement-fixing antibody to the soluble A antigen in 80% of the serums of 80 patients who were convalescing from influenza with or without complications during the 1957 epidemic of Asian influenza in Sheffield, England. In 47 students hemagglutination-inhibition tests on serums taken after the epidemic showed that 20% of infections were asymptomatic. Six of 322 serums collected before the epidemic contained inhibitor to the Asian virus; 283 (44%) of 637 serums collected after the epidemic in Sheffield contained inhibitor, the number varying between 16 and 71% in persons of different ages. Pools of serums collected before 1957 and assembled by age showed no hemagglutination-inhibiting antibody to the Asian virus. Similar pools of serums collected after the epidemic showed antibody in amounts varying within wide limits. Probably at least half of the population had been infected during the epidemic. Hemagglutination-inhibiting antibody against the Asian virus appeared in the serums of 8 to 168 persons vaccinated with "A prime" and polyvalent vaccines but was not detected in the serums of 11 patients who had had influenza before 1957.

The authors feel that the finding of inhibitor to the Asian virus in 6 of 322 serums collected before the epidemic has to be considered in association with the appearance of inhibitor in 8 of 168 persons immunized with various influenza-virus vaccines which did not contain Asian virus. In this connection they mention Mulder's observation that antibody to the Asian virus was present in the Netherlands in some aged persons before the epidemic and was rare in persons aged less than 80 years. Mulder also observed the development of antibody after immunization with an influenza vaccine which did not contain the Asian strain. The observations of these authors do not entirely conform with Mulder's view that the Asian virus is essentially the virus responsible for the 1890 pandemic. An alternative explanation is that the Asian virus shares a minor antigenic component with some of the influenza viruses experienced before 1957. This minor component might represent the survival of a major antigen from some virus causing a human pandemic in the past. It could form the basis for a genetic variation in which the minor component had become the major antigen recognized in 1957 as that of the Asian virus.

Rupture of Diseased Large Arteries in the Course of Enterobacterial (Salmonella) Infections. F. G. Zak, L. Strauss and I. Saphra. New England J. Med. 258:824-828 (April 24) 1958 [Boston].

The histories of 11 patients are presented, which illustrate the syndrome of rupture of previously diseased large arteries in the presence of bacterial infection. The pertinent features, which are summarized in a table, show a predominance of men (9 men and 2 women) in the older age groups; all except 1 of the patients were over 55 years of age and 5 were over 70. Fever and leukocytosis were present in almost all cases, whereas typical gastroenteric symptoms occurred in less than half. In keeping with the numerical increase of atherosclerotic aneurysms over syphilitic ones, all but 1 case fell into the former category. In the concluding summary, the authors emphasize that the aorta and its major branches, particularly the iliac and femoral arteries, when the site of severe atherosclerotic changes and complicated by aneurysm formation, may become infected by gram-negative enterobacteriaceae, particularly Salmonella organisms, in the absence of bacterial endocarditis. They point out, though, that it would be unreasonable to assume that only the aorta and its major branches may be involved in this kind of bacterial infection. There is evidence in the literature that diseased arteries are susceptible to bacterial inflammation, as is the previously damaged heart valve. Well known are cases of infected aortic coarctation, patent ductus arteriosus, and arteriovenous aneurysms. The authors know of cerebrovascular accidents in the course of septicemias due to Salmonella organisms but are not aware of adequate microscopic studies of the incriminated arteries. Osteomyelitis of the lumbar spine may play an important part when the lower aorta is involved. The lengthening of the life span and its concomitant increase of degenerative arterial disease, coupled with a poorly understood increase of salmonellosis, will bring more cases of this syndrome to the attention of clinicians and pathologists.

The Importance of the Morphologic Blood Picture for the Diagnosis of Metastatic Neoplasms in the Bone Marrow. G. J. H. Den Ottolander, M. Pelt, H. B. A. Hellendoorn and J. Gerbrandy. Nederl. tijdschr. geneesk. 102:515-521 (March 15) 1958 (In Dutch) [Amsterdam].

In 120 patients with breast carcinoma, in whom metastasis had advanced to a point that the process could no longer be controlled by any therapeutic method, the following studies were carried out once or repeatedly: differentiation of leukocytes, hemoglobin content of blood, sedimentation speed of erythrocytes, alkaline phosphatase activity and calcium content of blood serum, excretion of calcium in the urine, biopsy of specimen from the iliac crest, and roentgenologic examination of the thorax and skeleton. Hematological changes, either single or multiple, were found in 36 of the patients. In the patients in whom the breast carcinoma had metastasized to the bone and bone marrow and in whom the blood picture was pathological, needle biopsy of the iliac crest yielded a considerably higher percentage of tumor tissue than in similar cases with a normal blood picture. In 11 patients with other malignant disorders, the presence of normoblasts in the peripheral blood was also associated with extensive tumor infiltration of the bone marrow.

In 14 patients with metastasizing breast carcinoma, an increase in the number of immature cells in the blood was associated with clinical deterioration. Clinical improvement during hormonal treatment was seen in 9 patients in whom the number of such cells decreased. In 1 patient with prostatic carcinoma, 2 patients with chronic myeloid leukemia, 2 with chronic lymphatic leukemia, and 2 with generalized Hodgkin's disease, the normoblasts disappeared from the peripheral blood when the clinical picture improved after treatment with drugs or with irradiation. The authors conclude that hematological changes in patients with malignant lesions are significant as an indication of extensive metastases in the bone marrow, as a prognostic symptom of the further course of metastases, and as a standard by which to judge the results of therapy.

Arsenic the Obscure. C. J. Rehling. J. M. A. Alabama 27:272-273 (April) 1958 [Montgomery].

The author cites histories to show why arsenic poisoning generally escapes medical attention. The early symptoms of arsenic poisoning resemble those of infectious gastroenteritis, and, when death does not ensue within a few hours, neurological symptoms appear. Such natural causes of death as infectious diarrhea are found listed on the death certificates of patients with arsenic poisoning who received medical attention. Laboratory tests on the urine have revealed arsenic in patients who survived the poisoning. Commonly classified as a cumulative poison, arsenic is excreated in the urine and feces for some weeks after ingestion of a toxic dose. It appears in the urine within a few hours, and rather simple sensitive toxicological tests can be readily performed in a laboratory to identify even very minute amounts. The Gutzeit test, or some modification thereof, is described in textbooks of clinical laboratory procedure and in standard toxicology textbooks for the identification of arsenic.

BOOK REVIEWS*

Ocular Allergy. By Frederick H. Theodore, M.D., Associate Clinical Professor of Ophthalmology, New York University Post-Graduate Medical School, New York, and Abraham Schlossman, M.D., Clinical Assistant Professor of Ophthalmology, College of Medicine, State University of New York, Brooklyn. With chapters by William B. Sherman, M.D., Associate Clinical Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, and Robert S. Coles, M.D., Instructor in Ophthalmology, New York University Post-Graduate Medical School. Cloth. $12. Pp. 420, with 113 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

There is no tissue as susceptible to allergic manifestation as the eye, especially the lids and conjunctiva. For this reason this book should be of interest to all ophthalmologists and allergists, who meet here on common ground. The first chapter, by William B. Sherman, deals with the basic principles of allergy, and the subsequent chapters describe in detail the various forms of allergy encountered in the lids, conjunctiva, cornea, sclera, uvea, lens, retina, and optic nerve. Differential diagnosis is well covered since, as the authors point out, the treatment should be quite different in in allergic and nonallergic diseases. They properly decry the common practice of which so many drug manufacturers and physicians are guilty—that of combining corticosteroids with antibiotics as a sort of "shot gun" therapy. As is well known, the use of cortisone and allied products in dendritic ulcer of the cornea may be disastrous to sight. The historical background of many of the conditions is well covered, and the book is adequately illustrated. The bulk of the material is noncontroversial, and the authors have approached the more controversial subjects, such as the role of allergy in uveitis, in a restrained and rational manner. Here they have followed Woods' classification of uveitis into granulomatous and nongranulomatous forms. Emphasis is placed on allergy to bacterial infection elsewhere as the important factor in the cause of the nongranulomatous form with consequent improvement under corticosteroid therapy, whereas this form of treatment is contraindicated in the granulomatous type where tuberculosis is a frequent cause. The concept of such entities as retrobulbar neuritis and central angiospastic retinopathy as essentially allergic reactions may be questioned but the authors have avoided extreme dogmatism. The advocacy of staphylococcic toxoid in the treatment of chronic blepharoconjunctivitis due to Staphylococcus as a desensitization mechanism is interesting as a revival of an old method of treatment that has not been widely used in recent years.

Van Nostrand's Scientific Encyclopedia: Aeronautics, Astronomy, Botany, Chemical Engineering, Chemistry, Civil Engineering, Electrical Engineering, Electronics, Geology, Guided Missiles, Mathematics, Mechanical Engineering, Medicine, Metallurgy, Meteorology, Mineralogy, Navigation, Nuclear Science & Engineering, Photography, Physics, Radio & Television, Statistics, Zoology. Third edition. Cloth. $30. Pp. 1839, with illustrations. D. Van Nostrand Company, Inc., 120 Alexander St., Princeton, N. J.; 257 Fourth Ave., New York 10; D. Van Nostrand Company, Ltd., 358 Kensington High St., London, W. 14, England; 25 Hollinger Rd., Toronto 16, Canada, 1958.

This one-volume encyclopedia is a collection of terms that are fundamentally of interest to scientists. It is the work of 36 contributors, including men from educational institutions, research centers, and industry. About 15,000 terms are defined and explained, and some broad aspects are developed at length. Each term which might be used in the explanation of a second term is set in bold face type in the body of the article. This permits a reader to obtain supplementary information on a topic and, at the same time, the economical use of the limited space demanded by a book of this nature. The volume also contains numerous illustrations, diagrams, and charts which aid in condensing some of the material, but some of the reproductions leave much to be desired as far as clarity is concerned. Usually, the terms are first defined briefly and simply and then, if necessary, more detailed and technical information is given. This enables both the novice and the trained technician to benefit from the book. Since the coverage is so broad, a one-volume encyclopedia of this type must be selective in the material chosen. Frequently, therefore, one does not find a particular field covered as thoroughly as might be wished.

An Introduction to Experimental Surgical Studies. By W. J. Dempster, F.R.C.S., Lecturer in Experimental Surgery, Postgraduate Medical School of London. Cloth. $10. Pp. 463, with 73 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

This book is intended for the postgraduate surgical student who is interested in experimental surgery. The author has wisely used the clinical problem as his starting point. For such an approach however, it must be assumed that the researcher has had some surgical training, for this work does not recapitulate the essentials of surgery. No attempt has been made to describe experimental procedures in detail, but the principles of these procedures are indicated. The book is well documented, as it is also intended as a guide to experimental literature. It is emphasized throughout that the protocols pertaining to a given problem must be read first-hand in order to avoid a wrong interpretation of another author's work. This admonition is commendable. The author has attempted throughout the book to dovetail the work of the clinician and the animal experimentalist. Much of the book discusses healing, tissue regeneration, grafting, transplanting, and implanting. This phase of the book is particularly well done. Chapter 6, which deals with cardiovascular problems, is somewhat abbreviated and probably will be enhanced in future editions as knowledge of this modern field of surgery broadens. This book can be recommended to anyone interested in experimental surgery.

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*These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

Tuberculosis in White and Negro Children. Volume I: The Roentgenologic Aspects of the Harriet Lane Study. By Janet B. Hardy, M.D.C.M. **Volume II: The Epidemiologic Aspects of the Harriet Lane Study.** By Miriam E. Brailey, M.D., Dr.P.H. Cloth. $7.50; $4.50. Pp. 122; 103, with illustrations. Published for Commonwealth Fund by Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E. C. 4, England, 1958.

The introduction to volume 1 is devoted to the definition of the basic terms used in the legends which accompany the roentgenograms depicted. The pulmonary, segmental, and lymphatic anatomy is briefly but adequately reviewed. The major portion of this work is an atlas of roentgenograms with accompanying explanations which depict the various stages and forms of pulmonary tuberculosis. The serial film studies are particularly instructive. Some of these predate the chemotherapeutic era, whereas others show the effects of specific chemotherapy. On occasion the roentgenograms are supplemented by bronchoscopic findings or autopsy material. Representative roentgenograms of osseous tuberculosis are also presented. The differential diagnosis of tuberculosis in children from the radiologic standpoint is also dealt with. The indications, contraindications, complications, and method of bronchoscopy and bronchography are discussed in detail. This volume should be of general interest, but it is of particular value to radiologists, pediatricians, and physicians interested in pulmonary tuberculosis.

Volume 2 is based on a study performed at the Johns Hopkins Hospital Outpatient Department between 1928 and 1944, with some observations continued until 1950 and some predating antimicrobial therapy. The total picture of infected children differs in size and in epidemiologic characteristics from place to place. Children in a given urban area show great variation in the prevalence of tuberculin sensitization. Section 1 deals with the prognosis of tuberculosis among white and Negro children in congested urban areas. Morbidity studies were made by an analysis of chest x-ray findings at the time infection was discovered and were followed through in the various age groups. Of the white and Negro children between 5 and 15 years of age at the discovery of infection, about 33% showed involvement of the tracheobronchial lymph nodes. Parenchymal lesions of any kind were seen in less than 2% of the white children, but gross parenchymal involvement of the childhood type was seen in 5% and reinfection with pulmonary tuberculosis in more than 1% of the Negroes. Over a 15-year period the case fatality rate in white children who were infected before the age of 3 years was about 9% and in the corresponding group of Negro children nearly 22%. The fatality rates were not significantly different for male and female children of the same race and of comparable age when infection was discovered. Section 2 deals with the risk of developing reinfection with pulmonary tuberculosis. The basic criteria used for a diagnosis of this condition were roentgenograms, but the clinical course was also taken into account. Among the interesting and informative studies concerning reinfection with pulmonary tuberculosis, the author states that of 434 infected white children observed for 5,930 person-years only 2 (0.34%) showed evidence of reinfection, in contrast with 858 infected Negro children, observed for 9,732 person-years, of whom 32 developed progressive pulmonary tuberculosis. The incidence was nearly 10 times that for white children in this study. In susceptible subjects, notably in children of Negro stock, superinfection increased the risk in the development of tuberculosis. These two volumes are highly recommended for the physician, social worker, and lay person interested in tuberculosis.

Surgery of the Chest. By Julian Johnson, M.D., D.Sc., Professor of Surgery, School of Medicine and Graduate School of Medicine, University of Pennsylvania, Philadelphia, and Charles K. Kirby, M.D., Assistant Professor of Surgery, School of Medicine, University of Pennsylvania. Handbook of operative surgery. Second edition. Cloth. $9.75. Pp. 398, with 86 illustrations by Edna Hill. Year Book Publishers, Inc., 200 E. Illinois St., Chicago, 1958.

Those familiar with the first edition of this excellent textbook do not need to be told of the virtues of the work, and those who are unfamiliar with it, if they are engaged in the practice of thoracic surgery, should profit by keeping it handy as a reference book for reviewing the anatomy of the pulmonary hilus. It deals only with the techniques of the operations, and this phase of the subject is not slighted, as is so often the case in general textbooks in which the major emphasis is on the diagnosis and the indications for operation. It is brief and to the point, and the illustrations are adequate.

QUESTIONS AND ANSWERS

INTERMITTENT ALBUMINURIA

To the Editor:—*An adolescent boy with intermittent albuminuria but no evidence of kidney disease was given a diagnosis of orthostatic albuminuria. The question was raised as to whether spilling of seminal fluid into the urethra of a continent adolescent boy, at an age when his sexual hormones were very active, might cause a transient faint albuminuria. Has such a cause of albuminuria been proved or encountered frequently in similar cases?*

M.D., North Carolina.

Answer.—This consultant is unaware of any case in which albuminuria has been proved to be caused by the unconscious escape of seminal fluid. Such an event must be unlikely. The absence of factual data requires that the question be considered on theoretical grounds. Evidence to support the thesis that unconscious escape of seminal fluid occurs is scant. It has been reported, however, from a study of two patients, that spermatozoa could be demonstrated in about three-quarters of the daily specimens of urine of adult continent men who were examined. This evidence was offered to substantiate the theory that the seminiferous tract normally empties itself to some degree by means of a slow flow into the prostatic urethra independent of, and in addition to, ejaculation (Wilhelm and Seligmann, *Am. J. Surg.* 35:572, 1937). It would appear logical to assume, although it has not been proved, that if spermatozoa are discharged into the prostatic urethra unconsciously the other constituents of seminal fluid likewise may reach that site in a similar manner. Assuming that seminal fluid, which contains 2-6% protein, does escape unconsciously into the prostatic urethra, how much seminal fluid would be required to cause the urine to react positively for albuminuria? To answer this question, four different specimens of seminal fluid were added to urine in varying concentrations, and the urine was tested for albuminuria by the sulfosalicylic acid method. (Previously it had been determined that the urine reacted negatively for albuminuria.) It was established that in a volume of 100 ml. of urine it was necessary, in most of the specimens, to add 1 ml. or more of seminal fluid to obtain a grade 1 response for albuminuria. The unconscious escape of seminal fluid in such magnitude appears highly improbable. It would be advisable to examine a specimen of urine collected before the patient arises in the morning for albuminuria. It would appear logical to assume that, if an unconscious escape of seminal fluid occurs, a maximal amount would collect during the hours of sleep, when the patient has not urinated. If this specimen fails to react in a positive manner for albuminuria and if a positive result is obtained with urine collected after the patient has assumed the erect position, it may be concluded that orthostatic albuminuria is present and that the unconscious escape of seminal fluid plays no role in the albuminuria.

TREATMENT OF CHRONIC GLOMERULONEPHRITIS

To the Editor:—*What is the current opinion on the aspects of a fluid protein diet and steroid therapy in the treatment of chronic glomerulonephritis?*

Murray Russell, M.D., Garden Grove, Calif.

Answer.—The question is assumed to bear primarily on acute hemorrhagic glomerulonephritis (type 1 of Ellis). This syndrome usually, but apparently not always, appears in the wake of clinical infection or exposure to a "nephritogenic" hemolytic Streptococcus. An initial routine is therefore to obtain a culture of the nasopharynx or other possible sites of infection, to isolate the patient, and to provide adequate penicillin until the initial or subsequent cultures are negative. This may not directly help the patient, but it will prevent spread of the disease to others in the family. In diet, the current practice is to prescribe a low sodium diet (0.5 Gm. or less daily), restricting protein intake to less than 1 Gm. per kilogram of body weight only in the presence of azotemia, when also potassium (e.g., fruit juices) and phosphate (e.g., milk) intakes should be reduced. Fluid restriction is required only when there is oliguria; in general, intake is maintained at about 0.5 to 1 liter daily in excess of measured urinary loss. The variable course of this disease and the small number of patients followed by any single observer have led to a variety of views on the advisability, or, as some believe, inadvisability, of steroid therapy. In brief, there is no good evidence that steroids alone or in combination with nitrogen mustard will modify the initial phase of this condition. However, if at the end of some weeks (four to six) of room rest, the evidences of inflammatory activity seem to have

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

stabilized, even at a low level, this consultant's practice is to test over several days the response of proteinuria and urine sediment to therapy with prednisone (10-30 mg. daily, given orally). Should there seem to be a favorable response, in terms of decreased proteinuria, hematuria, and cylindruria, the steroid treatment is continued in gradually diminishing doses for three weeks, the course terminating with two to three daily doses of ACTH. Unfortunately, there is no proof that this regimen is of real value in cutting the total process short. As to chronic glomerulonephritis, it is customary to maintain sodium restriction and, if there is azotemia, protein restriction during the nephrotic phase, which also provides an occasion for a test of response to steroids. This response is commonly poor only with post-treatment or associated with diuresis. Advanced chronic glomerulonephritis with azotemia requires maintenance of water and electrolyte balances. Neither in this condition nor in subacute glomerulonephritis have favorable responses to steroid treatment been observed.

HIRSUTISM IN A YOUNG CHILD

To the Editor:—*A 7-year-old girl, with otherwise normal feminine and physical characteristics, has dark hair about 0.5 to 0.75 in. long all over her back and forearms. She has no pubic hair as yet. Is there anything to do about this except use a depilatory? What diagnosis could be given?*

M.D., Michigan.

Answer.—The hair growth on the back and forearms of a 7-year-old normal girl is undoubtedly nevoid in nature. The hairy pelt is known as a pilose nevus. It is one of the giant nevi and may or may not become pigmented as the youngster matures. The use of a depilatory is good conservative treatment. Permanent epilation may be obtained by electrolysis with destruction of the individual hair follicles, but this process is tedious, painful, and, according to some authorities, not entirely without danger in nevoid conditions.

Answer.—A moderate degree of hirsutism in the areas mentioned may occur without any demonstrable endocrine or other abnormality. In some cases the tendency is familial. However, Perloff (*J. A. M. A.* 157:651-652 [Feb. 19] 1955) reported on four children with hirsutism involving the upper half of the back and the extensor aspect of the extremities that was due to mild hypothyroidism. This cleared in three to six months with cautious thyroid therapy. There are a number of other endocrine causes of hirsutism, such as hyperpituitarism, Cushing's disease, hyperplasia or neoplasia of the adrenal cortex, adrenogenital syndrome, arrhenoblastoma of the ovary, and prolonged administration of ACTH. These usually are accompanied by other clinical evidence of masculinization or endocrine abnormality, so that they are unlikely in this child. Hirsutism may occur in porphyria and several neurological diseases, which should also give more definite associated clinical findings than this child shows. If no endocrine cause is found, the hair can be rendered less conspicuous and partially removed by regular bleaching with 20-vol. hydrogen peroxide rendered slightly alkaline with ammonia water. Temporary removal is best accomplished by application of a stiff wax, heated until soft, applied to the skin, and pulled off when hard. Such a wax can be made of 1 part of white wax to 4 parts of resin. According to Savill (Hair and Scalp, ed. 4, London, Edward Arnold & Co., 1952), this retards the subsequent growth of hair after several applications.

PLEURAL EFFUSION

To the Editor:—*A 20-year-old man was admitted to the hospital with a small pleural effusion in the left costophrenic angle. He was afebrile, and his white blood cell and differential counts were normal. His hemoglobin level was 15 Gm. per 100 cc.; his sedimentation rate was 28 mm. per hour. His chest x-ray revealed no evidence of parenchymal disease. The first test with purified protein derivative of tuberculin was negative, as were skin tests with coccidioidin and histoplasmin. The result of the second test with tuberculin P.P.D., however, was 2+ at 48 hours. He produced no sputum, and findings in gastric washings cultured for acid-fast bacilli were negative on three occasions. Aspiration of the pleural effusion on the left side revealed these data: red blood cells, 30 per cubic millimeter, and white blood cells, 7,950 per cubic millimeter, with polymorphonuclear cells, 39%, lymphocytes, 16%, and eosinophils, 45%. The protein level has not yet been reported. An insufficient quantity of fluid for specific gravity determination was obtained, but the sugar level on examination of this fluid was 28 mg. % and smears for acid-fast bacilli and for pyogenic organisms were negative. A second thoracentesis yielded the same information, except that on this occasion 90% of the cells were eosinophils. Please give an opinion concerning the causes of a small pleural effusion containing a predominance of eosinophils and, in addition, the significance of the low sugar level.*

M.D., South Carolina.

Answer.—A low sugar content of effusions into serous cavities is expected in infections due to tubercle bacilli. The glucose level is lowered by the glycolytic properties of the bacteria and the inflammatory cells. The fasting blood sugar level should be known in order to rule out a hypoglycemic state due to injected insulin or pancreatic adenoma. The relative number of eosinophils in the peripheral area should be determined. Eosinophils in any serous fluid may simply reflect a systemic eosinophilia due to allergy (from drugs, infections, skin irritants, or inhalants), Hodgkin's disease, polyarteritis, or trichinosis. Of particular interest is trichinosis, because of the well-known propensity for trichina to invade the diaphragm, an organ widely applied to the pleura. Further studies of the fluid could include culture for tubercle bacilli and injection into a guinea pig. Endoscopy of the bronchi and pleura may eventually be desirable. Pleural biopsy may also contribute to clarification.

INJECTABLE HEMOSTATIC PREPARATIONS

To THE EDITOR:—*In procuring an injectable hemostatic agent, what would be the best preparation to purchase?*

Frank A. Andrews, M.D., Coldwater, Mich.

ANSWER.—Since there are several basic causes of hemorrhage, it is easy to understand why no single hemostatic agent is known nor likely to be discovered that will effectively control all types of bleeding. Many agents are or have been acclaimed as effective hemostatics on an empirical basis without critical studies to establish their worth. Dependence on such empirical drugs can often lead to serious consequences because the bleeding condition is allowed to progress, whereas if a correct diagnosis had been made the bleeding could in many instances be treated specifically and effectively. Vitamin K has almost completely eliminated the hypoprothrombinemic bleeding of the patient with jaundice, the newborn baby, and the patient with sprue. This agent is ineffective in hemophilia, thrombocytopenic and nonthrombocytopenic purpuras, and even in the congenital types of hypoprothrombinemia. Cortisone and related compounds, such as prednisolone, often have a striking beneficial effect on controlling the bleeding in thrombocytopenic purpura. A temporary beneficial effect can also be obtained by a platelet transfusion. The most effective hemostatic is fresh plasma or plasma promptly separated from the cells, frozen, and stored at —20 C. Such a product has a wide therapeutic range since it temporarily corrects the coagulation defect in hemophilia, hemophilia B, congenital hypoprothrombinemia, hypofibrinogenemia, and other bleeding states. Lyophilized plasma is particularly valuable since it can be stored at room temperature and is readily reconstituted by the addition of distilled water. It has one disadvantage, especially if made from pooled plasmas, namely, of occasionally transmitting the virus of infectious hepatitis. In hypofibrinogenemia caused by premature separation of the placenta, retention of a dead fetus, or amniotic embolism, the intravenous injection of 2 to 4 Gm. of dissolved fibrinogen has been found effective in stopping uterine hemorrhage. Capillary bleeding which is characterized by continuous oozing is particularly troublesome to control. Several drugs, such as carbazochrome salicylate and conjugated estrogenic substances, have been claimed to control hemorrhage, but considerably more critical studies will be required to substantiate such claims.

HYPERURICEMIA

To THE EDITOR:—*Recently, a 49-year-old man with chronic kidney disease died from uremia. Autopsy revealed generalized gout with gouty nephritis. His only son has a serum uric acid level of 5.1 mg.%. What treatment should be given him? Should a low purine diet be used alone or in combination with probenecid with periodic determinations of the uric acid level?*

Parker W. Snyder, M.D., Peru, Ind.

ANSWER.—The question does not indicate whether a serum uric acid level of 5.1 mg.% is abnormally high by the method employed (it is by some methods but not by others). The unstated age of the son also is relevant, since hyperuricemia in males with the gouty trait does not usually appear until puberty. Assuming hyperuricemia to be present, it is advised that restriction of purines and avoidance of excessive protein and alcohol, together with liberal fluid intake, is all that should be recommended at this time. The serum uric acid level and the urine should be checked at intervals, without undue anxiety to the patient, who may well go through life with few or no difficulties due to gout. If there is ever any indication of tophaceous deposits or if the serum uric acid level is ever excessively high, probenecid should be given. It should be appreciated that, while uricosuric agents decrease the amount of uric acid reabsorbed by the renal tubules, they increase the amount excreted in the urine and the hazard of forming uric acid stones.

OSLER-WEBER-RENDU DISEASE (HEMANGIOMATOSIS)

To THE EDITOR:—*Is the Osler-Weber-Rendu disease usually generalized in distribution, or can local manifestations be present in a substantial number of cases? If the latter is true, how can the diagnosis of localized disease only be substantiated? How seriously does this condition affect mortality rates or longevity? Does or should this disease have an influence on insurance ratings?*

M.D., New Jersey.

ANSWER.—In Osler-Weber-Rendu disease (hemangiomatosis), both generalized and local distribution of telangiectatic lesions occur. The generalized type is more spectacular and, therefore, is more often described in the literature, but probably many patients with nosebleeds really have familial epistaxis. However, even those individuals with localized manifestations, such as melena or epistaxis, may have more widespread lesions which apparently are silent or, at any rate, from which bleeding does not occur to such an extent that symptoms or signs are produced. Obviously, one can never prove that the disease is localized as far as occurrence of telangiectases is concerned. The death rate from this disease is not great, but continued bleeding results in iron deficiency anemia and frequent epistaxis interferes with many normal activities. In a homozygous case, where both abnormal maternal and paternal genes are inherited (Snyder and Doan, *J. Lab. & Clin. Med.* 29:1211, 1944), bleeding may be overwhelming and death may occur in early life. In the opinion of this consultant, medical and insurance objectives do not necessarily coincide. From a medical standpoint, deaths from this condition occur not much above the normal rate. Patients rarely die from hemorrhage. However, some of these patients do have hepatic involvement, and cirrhosis has been reported (Smith and Lineback, *Am. J. Med.* 17:41, 1954).

METASTASIS FROM BLADDER CARCINOMA

To the Editor:—*A man, aged 71, was in very good general health except for a carcinoma of the bladder, grade 2, extensive enough to involve a good portion of the trigone. His condition was held in abeyance for five and one-half years by fulguration, implanting of radon seed, and x-ray. He then had severe, incapacitating pain in the lower part of the back, and x-ray showed moderate arthritis, with no evidence of metastasis from bladder involvement. He suddenly developed severe convulsions and died in about 12 hours. What are the routes of metastasis in carcinoma of the bladder? Could this bladder condition have caused the convulsions by metastasis to the brain? There were no premonitory mental disturbances.*

Lewis C. Calvert, M.D., Weston, Mo.

Answer.—Carcinoma of the bladder commonly metastasizes by the invasion of adjacent tissue and by spread to the adjacent lymph nodes. Distant metastasis to remote sites occurs rarely. It is possible but unlikely that the convulsions were caused by cerebral metastasis of the cancer of the bladder.

EXCESSIVE PROTEIN INTAKE

To the Editor:—*The answer to the question, "Are there any possible harmful consequences in the daily eating of one cup of cooked egg whites over a long period of time?" in the Questions and Answers section,* The Journal, *March 29, 1958, page 1663, might for completeness sake include the following experimental evidence. Human subjects placed on a refined diet containing a large amount of dehydrated egg white developed symptoms resembling those caused by biotin deficiency in animals. In experiments with rats, dermatitis, retarded growth, loss of hair, and loss of muscle control occurred when egg white was fed as the sole source of protein. Avidin, a protein in egg white, apparently combines with biotin and prevents its absorption from the intestine (Harper, Review of Physiological Chemistry, ed. 6, Los Altos, Calif., Lange Medical Publications, 1957).*

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The above comment was referred to the consultant who answered the original query and his reply follows.—Ed.

To the Editor:—*The writer of the comment is correct when he refers to the fact that there is experimental evidence indicating that human subjects placed on a refined diet containing a large amount of dehydrated egg white did develop symptoms very similar to those of a biotin deficiency in rats (Sydenstricker and others,* J. A. M. A. 118:*1199-1200 [April 4] 1942). The dehydrated egg white in this experimental diet amounted to about 200 Gm. per day and supplied about 30% of the total calories. Parenteral administration of a biotin product caused the symptoms to disappear within a very short time. This study has never been confirmed by others, and this fact may be related to the variability in intestinal synthesis of biotin in different subjects. It is pointed out, however, that dehydrated egg white which presumably had not received a severe enough heat treatment to destroy the avidin was used in this study. The question quoted in the comment referred specifically to "one cup of cooked egg whites." In this type of product, there would be no avidin present and one would not expect to observe any signs of biotin deficiency even with long-continued ingestion.*

USE OF MAGGOTS IN MEDICAL PRACTICE

To the Editor:—*Concerning the question and answer on use of maggots in medical practice which appeared in* The Journal, *March 29, 1958, page 1662, maggots used in this treatment do not attack live tissue. There is a maggot of the fly, Erythrocephala lata; this is the common screw worm and the larvae will and do attack live tissue, but they were never used therapeutically (McKeever,* J. Bone & Joint Surg. 15:85, *1933).*

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WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Congress Urged to Make Clear Ruling on VA Hospitalization . .

Nursing Homes Ask Congress to Authorize Mortgage Guarantees . .

Self-Employment Annuity Legislation Continues to Make Progress . .

CONGRESS ASKED TO RULE ON VA NONSERVICE CARE

Congress should come to grips with the problems of veteran hospitalization and state clearly that non-service-connected illness, if the veteran is indigent, is the responsibility of local government. This was the advice given the House Veterans Affairs Committee by the American Medical Association. The committee, headed by Chairman Olin Teague (D., Tex.), has been holding hearings for some weeks on Veterans Administration hospital policy and practices.

Dr. Russell B. Roth, of Erie, Pa., chairman of the A. M. A. Committee on Federal Medical Services, told the committee: "We believe that the Department of Medicine and Surgery of the Veterans Administration has a single prime purpose, that of providing care for service-incurred or aggravated disease or disability. It was not created by Congress as an instrument of scientfic research; it was not designed as a training ground for young doctors. And it was not intended as an agency for providing indigent medcal care to the veterans population."

Dr. Martin R. Steinberg, chairman of the American Hospital Association committee on veterans relations, who testified the same day as Dr. Roth, declared: "We believe the federal government should undertake to provide fully for all of the needs of veterans for any illness which is service-connected throughout his lifetime. We believe, however, that the federal government has no such responsibility with respect to non-service-connected conditions. . . . Congress should enact definitive legislation to provide hospital and medical care if such veterans are declared to be eligible and providing the need of care is established within a limited period after their separation from service."

The A. M. A. witness suggested that the veterans committee authorize a serious study by the General Accounting Office and the VA on the income level of non-service-connected cases, primarily those in general medicine and surgery hospitals. Dr. Roth said the A. M. A. Committee on Indigent Care study of local and state medical care plans reports that not "even one welfare department in the country will pay for a man's medical care purely on his unsupported statement that he can't afford it."

Dr. Roth also urged strengthening of the law to permit examination of the admission affadavit to VA hospitals (which non-service-connected patients must sign when declaring they are unable to pay for care elsewhere). Such form, he said, is "lightly considered in these times."

A. M. A. studies, the committee was told, indicate that 1 million dollars in a VA general medicine and surgery hospital will care for 1,696 veterans, while the same amount of money in a private hospital of the same type would care for 5,389 patients. "We do not believe that throwing away nearly 70 cents out of every dollar spent on this medical care is a reasonable financial course for this nation."

The AHA witness recommended, among other things, (1) that consideration be given to adding a new category of public assistance to the social security act for veterans with non-service-connected disabilities who can't meet the expense, (2) establishment of a coordinating agency in the federal government to assure proper planning and coordination of VA hospitals with other federal hospitals and in relation to nonfederal hospitals, (3) that discharged military personnel receive health insurance, with the government underwriting the premium as a severance benefit for a limited period of time.

At the outset of the hearings, Chairman Teague ventured the opinion that the country would never halt all non-service-connected care for veterans, and he said further that he doubted that any member of Congress would introduce a bill to that effect.

Witnesses from the Oklahoma Medical Society also recommended a closer liaison between medical societies, medical schools, and local VA hospitals "so that there will be more mutual awareness and early solution of common local problems." Witnesses were Drs. J. R. Stacy, Mark R. Johnson, and Harold G. Sleeper.

NURSING HOME ASSOCIATION RENEWS APPEAL FOR LOAN GUARANTEES

Hearings on federal mortgage guarantees for proprietary nursing homes have concluded, with the final witnesses representing the American Nursing Home Association. The spokesmen—George T. Mustin, a past-president of the association; Mrs. Goldie Rogers, of the Maryland association; and Charles Dunn, head of the Alabama association—

appeared before a subcommittee of the House Banking and Currency Committee, renewing an appeal made earlier before a Senate committee.

Legislation authorizing U. S. guarantee of loans passed the Senate and is pending before the subcommittee.

Mr. Mustin made these points, among others:

Proprietary homes care for "the vast majority" of nursing home cases, and "there is no expectation whatever that nonprofit or public institutions can or ever expect to take over the full responsibility for the aged."

The nursing home is a small, taxpaying business of real service to the community, yet it has difficulty obtaining the usual commercial type mortgage because it is a one-purpose structure.

Nursing homes are not asking for subsidies; they will pay the going rate of interest and repay the loans, so the money can be used "over and over again."

Nursing homes serve "hundreds of thousands of elderly patients who otherwise would be forced to enter general hospitals and pay the relatively high prices that hospitals are forced to charge."

Commenting on recommendations made earlier by spokesmen for the American Hospital Association, Mr. Mustin said that while the Public Health Service's nursing home definition probably would be satisfactory with certain changes, care should be taken not to "abrogate" states' right to license and regulate these facilities. He also pointed out that surveys of nursing homes, proposed by the AHA to establish community need, would be unnecessary because protection of the risk capital would insure that a need existed before the home would be built.

JENKINS-KEOGH BILL REPORTED OUT BY WAYS AND MEANS COMMITTEE

Jenkins-Keogh legislation to help the self-employed save for their retirement years is one step farther along the road toward enactment. It has cleared the House Ways and Means Committee.

As reported out of the committee, the bill carries the following provisions:

Eligibility: All those subject to the social security self-employment tax, plus physicians and some other categories of self-employed not now covered by social security.

Deduction Limit: Deduction is limited to 10% of net earnings but not over $2,500 a year and not over $50,000 lifetime setaside, because the program is limited to 20 years. Those 50 years of age or older when the law goes into effect may deduct an additional amount each year, but no deductions are to be allowed after age 70. (A lower lifetime limit is imposed for those who have been or are at any time covered by employer-sponsored retirement plans.)

Policy Restrictions: If a combined annuity-life insurance program is selected, only the money allocable to retirement may be deducted.

Trustee Provisions: Only a bank may be a trustee of the funds, and trust investments are restricted to certain public securities. The trust will be tax exempt. The trust may pay out at any time—with a tax penalty if paid prior to age 65—but payment must begin by age 70 and be completed by age 80.

After House passage, it still must pass the Senate.

Another possibility for this form of tax relief is a small business assistance bill that now is before the Senate Finance Committee. One section provides Jenkins-Keogh type tax deferment but under a different arrangement than the House bill. The Senate bill would limit the setaside to $1,000 per year and cover, in addition to the self-employed, all employed who do not benefit from an employer-sponsored pension plan. A small business bill without this provision already has passed the House.

HALF OF COUPLES RECEIVING OASI HAVE TOTAL INCOMES OF $2,190

A preliminary report based on a survey shows half of the retired couples receiving social security benefits had total incomes of $2,190 last year, and half had less than that amount.

The findings are from a nationwide survey of about 5,000 couples, regarded as a scientific cross-section of the 11 million persons now receiving old age and survivors insurance.

Aside from OASI benefits, the couples had outside income according to the following pattern: 19% were receiving less than $75 for the year, 28% less than $200, 50% more than $900, 32% more than $1,500, and 13% more than $3,000. Outside income from all sources was taken into account, including public assistance payments.

This particular study was concerned only with income and did not take into consideration financial holdings. At the completion of the survey, this information will be compiled, as well as data on retired persons' availability for and attitudes toward employment and their expenditures.

MISCELLANY

The National Science Foundation will receive applications for postdoctoral fellowships through Sept. 2, with awards to be announced Oct. 15. Candidates must be citizens of the United States with special aptitudes for advanced training and must have their doctor's degree or the equivalent in training and experience.

A conference on staphyloccocic disease will be held at the PHS Communicable Disease Center in Atlanta, Sept. 15-17.

The Joint Blood Council, Inc., has established standards for evaluating and comparing policies and technical procedures of blood transfusion services. Dr. Leonard W. Larson, chairman of the A. M. A. Board of Trustees and newly-elected president of the council, invited blood banks to use the standards "for voluntarily evaluating themselves." Full details are available from the council, located at 1832 M Street, N. W., Washington 6, D. C.

The United States will contribute $350,000 toward cost of a nuclear research reactor project to be erected in Norway for medical and other research and development. It is the 16th similar grant to be made under President Eisenhower's Atoms for Peace program.

THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 14

CHICAGO, ILLINOIS

AUGUST 2, 1958

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THROMBOLYSIS WITH FIBRINOLYSIN (PLASMIN)—NEW THERAPEUTIC APPROACH TO THROMBOEMBOLISM

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Fifty-two patients with various forms of thromboembolic disease were treated by intravenous infusions of a preparation of fibrinolysin in dosages up to 90,000 fibrinolytic units (FU). The resulting increase in the fibrinolytic activity of the patient's plasma was demonstrated by laboratory determinations of the rate of dissolution of a standard fibrinogen-thrombin clot. When the dosages were between 40,000 and 50,000 FU, 92% of the recipients manifested an enhanced plasma fibrinolytic activity at some time after the infusion. Ten case histories illustrate the symptomatic relief that generally followed the infusion. Hemorrhagic complications have not occurred, and disturbances of the blood-coagulating factors were minimal as measured by prothrombin time, recalcification time, prothrombin content, proconvertin content, proaccelerin content, and fibrinogen content. Fever followed the infusion in 25 patients, and delayed allergic skin reactions occurred in 2; these were the most significant side-effects. The results encourage further trials in cases of thromboembolic disease of peripheral, cerebral, and coronary vessels.

Despite improved diagnostic and therapeutic techniques, thromboembolism maintains its unwelcome position as one of the major causes of medical morbidity and mortality. It has become apparent that the anticoagulant drugs do not provide a definitive answer to this problem. While the extension of existing thrombosis, or its recurrence, may be favorably influenced by these agents, the original thrombus remains. The organism is left to its own devices in dealing with this occlusive mass. Such devices rarely act with sufficient speed and intensity to prevent tissue damage, even though recanalization may be achieved eventually.

In recent years, therefore, much attention has been directed toward a class of materials grouped together under the term fibrinolytic agents. These compounds share the ability to promote the dissolution of the fibrin framework on which a thrombus is supported. By exerting fibrinolytic effects within the vascular system, such agents should be capable of acutely dissolving thrombotic material. The ability to achieve rapid thrombolysis, combined with anticoagulant drugs, would appear to constitute "ultimate therapy" in thromboembolic states.

Perhaps the first fibrinolytic agent to attract attention was streptokinase. This material, first demonstrated in the filtrates of beta-hemolytic streptococcic cultures by Tillett and Garner in 1933,[1] is still an object of active investigation. While fre-

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quently regarded as a fibrinolytic substance, streptokinase has no direct action on fibrin. Rather, it functions as an activator of the plasma proenzyme, profibrinolysin (plasminogen), either by direct action or by converting a plasma proactivator to an activator.[2] By such action, streptokinase converts profibrinolysin to the active fibrinolytic enzyme fibrinolysin (plasmin). Therefore, the effect of streptokinase is dependent on the presence and concentration of profibrinolysin.

Table 1.—*Composition of Patient Group, by Disease*

	Patients, No.	Infusions, No.
Active deep thrombophlebitis		
With pulmonary embolism	3	5
Without pulmonary embolism	15	16
Pulmonary embolism from unknown source	8	11
Arterial occlusion		
Cerebral thrombosis	12	13
Internal carotid thrombosis	2	3
Coronary thrombosis	1	1
Brachial arterial embolus	1	2
Radial arterial thrombosis	1	1
Popliteal arterial embolus	1	1
Retinal arterial thrombosis	1	1
Superficial thrombophlebitis	7	7
	52	61

Unfortunately, inhibitors of streptokinase are present in a significant portion of the population, probably as a consequence of the ubiquity of streptococcic infections.[3] The presence of antistreptokinase factors in the plasma not only may increase the risk of allergic reaction but also would tend to limit the frequency and intensity of fibrinolytic activity which can be achieved by streptokinase infusion in the human body. The most purified preparations of streptokinase available still retain toxic potential and appear to provide an unreliable method for achieving plasma fibrinolytic activity in man at well-tolerated dosage levels.[4] Since both allergic and inhibitory phenomena are likely to be enhanced by streptokinase administration, the therapeutic value of this agent becomes subject to question.

Other workers have explored the use of the enzyme trypsin as a thrombolytic agent. This proteolytic enzyme not only can lyse fibrin directly but also serves as an activator of profibrinolysin.[5] However, the intravenous infusion of trypsin has not consistently led to the dissolution of thrombi in experimental animals or in man.[6] Furthermore, considerable antitryptic activity resides in both animal and human plasma.[7] Doses of trypsin which can overcome this inhibitor activity and produce reliable fibrinolytic effects also may have potent action against many of the protein components of plasma, including those necessary for blood coagulation.[7] These considerations appear to render intravenously given trypsin unsuitable as an agent for achieving acute dissolution of the intravascular clot in man.

As it became evident that streptokinase and trypsin had a number of theoretical and practical limitations as thrombolytic agents, interest became centered on fibrinolysin itself as a possible therapeutic weapon. While the presence of this intrinsic fibrinolytic agent in the blood of man and other mammalian species had been demonstrated before the turn of the century, only recently did technological advance permit its satisfactory isolation from human and bovine plasma. By modern biochemical procedures, profibrinolysin can be obtained from the globulin fraction of the plasma proteins.[8] Activation of this material to fibrinolysin is readily achieved by small amounts of streptokinase, which can be removed subsequently.

Since fibrinolysin has become available for investigational use, a number of important facts relating to it have become established. Unlike trypsin, intravenously given fibrinolysin does not attack a variety of plasma proteins with equivalent effect. Rather, it chooses fibrin as its major target of enzymatic activity.[9] This specificity of attack appears related to the fact that fibrin actually adsorbs fibrinolysin.[10] These qualities allow this agent to achieve satisfactory intravascular fibrinolytic activity in animals without disturbance of the coagulative mechanism over a wide dosage range.[12] Furthermore, several workers have shown that infusion of fibrinolysin will consistently dissolve experimentally produced arterial and venous thrombi in the dog and the rabbit.[13] Toxic reactions to effective intravenous doses of fibrinolysin in these experimental animals have been infrequent and minor.[13]

These observations have suggested that fibrinolysin may satisfy the major criteria for the ideal fibrinolytic agent, viz., the ability to achieve rapid liquefaction of intravascular clot without undue toxic effects.

In early 1957, a detailed study of the toxic and therapeutic effects of fibrinolysin in the human was begun at the District of Columbia General Hospital. To date, 52 patients with various forms of thromboembolic disease have received one or more intravenous infusions of fibrinolysin. This preliminary report is a summary of the major observations made during this period of investigation.

Table 2.—*Incidence and Degree of Febrile Response to Fibrinolysin Infusion*

	Infusions	
Peak Postinfusion Temperature Rise, Degrees Fahrenheit	No.	%
0-1	31	50.8
1-2	11	18.0
2-3	8	13.1
3-4	8	13.1
>4	3	5.0

Materials and Methods

Patients.—The 52 cases included in this study encompass all forms of thromboembolic disease (table 1). All patients treated were inpatients at the District of Columbia General Hospital between February and December, 1957.

Fibrinolysin.—The profibrinolysin used in this study is a highly purified derivative of human plasma protein fraction 3. It is activated to fibrinolysin (Actase) with small amounts of purified streptokinase, after which the residual streptokinase is removed. The activated material is then lyophilized, in which form it is stable for several months at −4 C. One fibrinolytic unit of fibrinolysin has been defined as that amount of a standard preparation which will change the turbidity of a standard fibrinogen-thrombin clot by 50% in 10 minutes.

The dosage of fibrinolysin was gradually increased as the study progressed. Thirteen patients received infusions of 30,000 fibrinolytic units (FU); 19 patients, 40,000-50,000 FU; and 20 patients, 69,000-90,000 FU. Nine patients received two infusions on separate days, so that infusions totaled 61.

TABLE 3.—*Incidence of Fever Related to Extent of Thrombosis Present*

Thrombotic Disease*	Infusions, No	Febrile Reactions No	Febrile Reactions %
Major			
Active deep thrombophlebitis	21	13	
Pulmonary embolization	11	6	
Superficial thrombophlebitis	7	4	
Total major disease	39	23	59
Minor			
Cerebral thrombosis	13	4	
Internal carotid thrombosis	3	1	
Radial artery thrombosis	1	1	
Brachial artery embolus	2	1	
Popliteal artery embolus	1	0	
Coronary thrombosis	1	0	
Retinal artery thrombosis	1	0	
Total minor disease	22	7	32

* "Major" and "minor" refer to probable amount of thrombotic material present, not to functional consequences of thrombosis

Plan of Study.—Fibrinolysin was dissolved immediately prior to use in 500 to 1,000 cc. of 5% dextrose in water. Intravenous infusion was then carried out over a two-to-four-hour period Base-line and serial postinfusion blood samples were studied as follows: one-stage prothrombin time,[14] plasma recalcification time,[14] fibrinogen content,[15] and plasma fibrinolytic activity in all samples; prothrombin content,[16] factor V (proaccelerin),[16] and factor VII (proconvertin)[16] in all samples from 35 patients; and hematocrit value and white blood cell count before and 24 hours after infusion. Temperature, pulse rate, and blood pressure were measured at three-to-four-hour intervals in all patients for at least 24 hours after infusion. Urinalyses and electrocardiograms were obtained before and 24 hours after fibrinolysin infusion in all patients. In 18 patients electrocardiograms were also obtained during or shortly after infusion. The clinical course of each patient was carefully followed throughout hospitalization and at subsequent visits to the outpatient department.

Toxicity

Fever.—A temperature elevation of 1 F or more occurred in 49.2% of patients receiving fibrinolysin (table 2). The febrile reaction usually began 6 to 8 hours after infusion, reached an average peak of 2.9 F (range, 1.0-5.2) at 10 hours, and declined to normal within the next 10 hours. Approximately 25% of these patients experienced some chilliness or nausea at the peak of the febrile response.

TABLE 4.—*Percentage of Patients Showing Abnormality in Blood Factors Three, Six, and Twenty-four Hours After Start of Fibrinolysin Infusion*

	3 Hr	6 Hr.	24 Hr
Prothrombin time, prolongation	42.4	44.1	40.3
Recalcification time, prolongation	30.8	29.3	40.4
Prothrombin content, depression	33.5	44.4	50.0
Proconvertin content, depression	36.7	21.2	36.7
Proaccelerin content, depression	26.7	37.1	25.0
Fibrinogen content, depression	64.5	53.1	37.9

Febrile response did not correlate, in either incidence or degree, with size of fibrinolysin dose or amount of fibrinolytic activity achieved in the plasma. However, the incidence of fever was significantly higher among those patients in whom extensive thrombotic material may be presumed to exist (table 3). No patient received medication designed to prevent or limit the febrile response. More recent experience had indicated that the febrile responses can be prevented or markedly ameliorated by aspirin-antihistaminic prophylaxis.

Blood Pressure and Pulse Rate.—No significant blood pressure deviations followed fibrinolysin infusion at any dosage level. Tachycardia occurred only in patients with pyrogenic reactions.

Allergy.—Two instances of allergic reaction developed on the third day after fibrinolysin infusion, one characterized by erythema at the site of infusion and the other by generalized urticaria. Both responded promptly to local measures and antihistamines.

Effects on Coagulation.—In the doses used, intravenously given fibrinolysin did not compromise the integrity of the coagulation mechanism. Prothrombin time and content, plasma recalcification time, and proconvertin and proaccelerin contents remained stable after infusion in the majority of patients (table 4). At no time interval did the average values for any of these factors fall below 90% of base-line values (table 5). A majority of

TABLE 5.—*Average Change in Coagulation Parameters and Factors* Three, Six, and Twenty-four Hours After Start of Fibrinolysin Infusion†*

	3 Hr	6 Hr	24 Hr
Prothrombin time, sec	+0.3	−1.7	−2.7
Recalcification time, %	107.0	105.1	92.5
Prothrombin content, %	94.6	91.5	91.6
Proconvertin content, %	94.5	95.5	90.1
Proaccelerin content, %	94.3	91.4	97.8
Fibrinogen content, %	88.3	90.2	100.4

* Reported as % activity, taking base-line values as 100%
† Values represent average of total group

patients did show some depression of fibrinogen content at three and six hours after infusion. However, the average fibrinogen loss was small, and base-line values had been reached or exceeded in most patients by 24 hours after infusion. There was no statistically significant tendency toward greater loss of coagulation factors as fibrinolysin dosage was increased.

Table 6.—*Percentage of Patients with Enhanced Plasma Fibrinolytic Activity Three, Six, and Twenty-four Hours or at Any Time After Fibrinolysin Infusion*[*]

Dosage, Fibrinolysin Units	Infusions, No.	3 Hr.	6 Hr.	24 Hr.	Any Time[†]
30,000	14	78.6	42.8	28.6	85.7
40,000-50,000	24	75.0	62.5	41.7	91.7
69,000-90,000	23	73.9	60.9	78.3	86.9
Total	61	75.4	57.4	52.5	88.5

[*] Enhanced activity is present when plasma would dissolve standard clot in 10% less time than that required by base-line plasma sample.

[†] Enhanced activity in at least one postinfusion sample.

These laboratory studies, indicating minimal disturbance of coagulation factors, correlated well with the clinical observation that no instance of hemorrhage was noted in any patient who received fibrinolysin, including 29 who were simultaneously receiving coumarin drugs or heparin. Possible "silent" internal hemorrhage appears excluded by the stability of the hematocrit values measured before (34.9%) and 24 hours after (34.3%) infusion.

Electrocardiogram.—In two patients electrocardiographic abnormalities were seen after fibrinolysin infusion. A 79-year-old woman with arteriosclerotic heart disease and mild cardiac decompensation developed atrial fibrillation 14 hours after fibrinolysin infusion, and a 27-year-old man with iliofemoral thrombophlebitis developed transient T-wave changes about 8 hours after infusion. In both patients, these changes occurred near the peak of significant febrile reactions.

Urinalysis.—No urinary sediment abnormalities occurred after fibrinolysin infusion. Transient, mild (1+, 2+) proteinuria occurred in 10 patients, all of whom had had febrile reactions to infusion.

Delayed Toxicity.—Periods of follow-up observation have extended from two weeks to eight months; no form of delayed toxicity has occurred.

Fibrinolytic Activity

The primary objective of intravenous fibrinolysin infusion is to achieve a level of plasma fibrinolytic activity which may be capable of dissolving an intravascular thrombus. Several methods can be used to detect such activity. The procedure used in this laboratory is a direct test of the ability of a plasma sample to dissolve a standard fibrinogen-thrombin clot. Increase in fibrinolytic activity is reflected by a more rapid lysis of the standard clot.

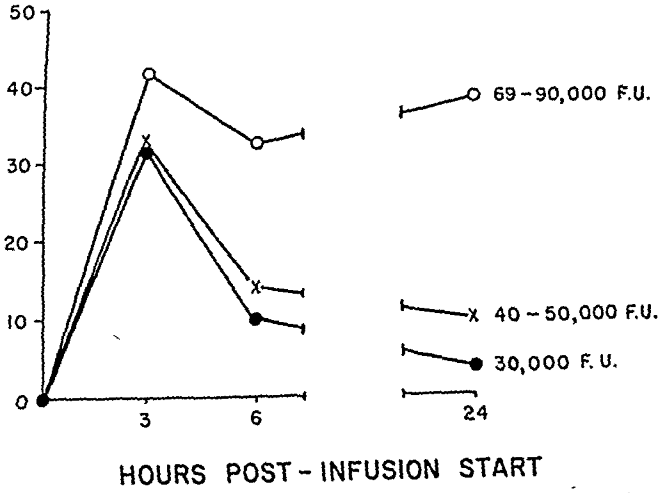
With this method it has been possible to demonstrate that fibrinolysin consistently produces a significant degree of fibrinolytic activity in the circulating plasma (table 6). The intensity and duration of fibrinolytic activity was a function of fibrinolysin dosage (see figure). At levels of 69,000 fibrinolytic units or more, high degrees of lytic activity are usually present for 6 to 8 hours and considerable activity frequently persists for 24 hours.

Therapeutic Observations

Deep Venous Thrombophlebitis.—Eighteen patients with deep venous thrombophlebitis involving the lower extremities received one or more infusions of fibrinolysin (table 1). Thirteen of these patients received anticoagulant therapy simultaneously or subsequently (see under Comment). Three patients in this group had suffered one or more pulmonary embolisms prior to fibrinolysin therapy.

Results of fibrinolysin infusion in this uncontrolled series have been consistently encouraging. While individual patients showed moderate variation in rapidity and degree of response, the over-all experience has included (1) loss of heat, tenderness and muscle turgidity, and significant decrease in leg size, by measurement, within 24 hours; (2) return of the involved area to its prephlebitic state within 72 hours after infusion; and (3) no recurrence of signs of phlebitis when ambulation was allowed. No pulmonary emboli occurred after fibrinolysin therapy. The following three case reports from this series illustrate the response of patients with deep venous thrombophlebitis.

Case 1.—A 58-year-old man, who was receiving chemotherapeutic agents for inoperable carcinoma of the lung, developed an acute iliofemoral thrombophlebitis of the right leg. The entire extremity became swollen, hot, and painful, with dilatation of superficial veins over the lower part of the leg. The patient was unable to walk. Therapy with bed rest and leg elevation was instituted. Anticoagulant drugs were withheld because of recent episodes of hemoptysis. After five days of such therapy, only slight improvement had occurred.



Average enhancement of plasma fibrinolytic activity after fibrinolysin infusion at three dosage levels. Percentage of increase (*vertical column*) of plasma fibrinolytic activity = $\frac{\text{(base-line lysis time)} - \text{(lysis time at x hours)}}{\text{(base-line lysis time)}} \times 100$

An intravenous infusion of 30,000 FU of fibrinolysin was carried out on the fifth day of his illness without evidence of toxicity. Twenty-four hours after infusion, the right leg had markedly decreased in size, averaging 3 cm. less by measurement in both calf and thigh. Heat and redness had subsided, and the patient tolerated deep palpation of the leg without pain. Two days after infusion, the extremity had returned to its prephlebitic state. The patient was ambulated 72 hours after infusion without recurrence of signs or symptoms. During a four-month period of observation, the leg has maintained its postinfusion improvement and the patient has continued to be ambulatory.

Case 2.—A 45-year-old man developed a cramp-like pain in the right calf 11 days before admission. This subsided after a day of rest at home. Nine days before admission the calf pain returned and was accompanied by heat, slight swelling, and moderate tenderness. Over the next several days, the process appeared to improve. However, the morning of admission the right calf became acutely swollen, hot, and extremely tender to touch and ambulation was impossible.

Examination revealed a temperature of 100.8 F (38.2 C) and a pulse rate of 100 per minute. The right calf was exquisitely tender, reddened, and hot. There was marked turgidity of the calf musculature, and the superficial veins were dilated. Homans' sign was present. The right midcalf circumference was 2.5 cm. greater than the left.

Eight hours after admission, 69,000 FU of fibrinolysin was infused over a two-hour period without evidence of toxicity. Six hours after infusion, therapy with heparin and bishydroxycoumarin was begun. Nine hours after the fibrinolysin infusion, heat and turgidity of the calf were much decreased. Superficial vein dilatation had subsided, and deep palpation of the calf now produced only questionable discomfort. Twenty-four hours after infusion, improvement had continued. Measurements then disclosed an 0.8-cm. difference between the two midcalf areas. Residual pain was confined to a small area just posterior to the internal malleolus, where a tender segment of thrombosed superficial vein could be felt. Seventy-two hours after infusion this area was no longer tender, although the venous segment remained palpable. The patient was ambulated and anticoagulants were gradually discontinued. Follow-up examination one month later disclosed no recurrence of signs or symptoms of venous disease.

Case 3.—A 67-year-old man with arteriosclerotic heart disease and chronic uremia developed marked swelling and tenderness of the left calf five days prior to admission. Two days before admission, the thigh also had become swollen and warm and calf swelling and tenderness had increased. Bed rest at home led to no improvement.

When the patient was admitted, the left leg showed a trace of pretibial edema and a turgid, quite tender left calf. The medial portion of the thigh was also firm, slightly tender, and warm. The left calf circumference was approximately 3.0 cm. greater than the right throughout, and the left thigh was approximately 2.5 cm. greater.

About 10 hours after admission, the patient received an infusion of 75,000 FU of fibrinolysin over a two-hour period. Heparin therapy was begun after completion of this infusion. Twenty-four hours later the turgidity, heat, and tenderness of both calf and thigh had subsided. The patient tolerated deep palpation with equivocal tenderness and moved the leg without pain. The leg had decreased approximately 2 cm. in average circumference in both calf and thigh.

By 48 hours after infusion, the leg showed no evidence of the phlebitic process. Heparin therapy was tapered over the next 36 hours, and the patient was considered ready for discharge insofar as the phlebitic episode was concerned. However, he remained in the hospital for further investigation of his renal status.

Pulmonary Embolism.—Eight patients with pulmonary embolism in whom no definite thrombotic source could be incriminated received fibrinolysin infusion within 72 hours of the embolic event. No untoward reaction, other than fever, followed infusion. In four patients a sequence of events suggesting that fibrinolysin therapy exerted some beneficial effect was noted. Criteria suggesting the influence of fibrinolysin included (1) rapid resolution of electrocardiographic abnormalities; (2) rapid relief of chest discomfort, tachypnea, and other symptoms and signs induced by embolization, and (3) interruption of a course of recurrent embolization which had not responded to anticoagulant therapy. Two representative cases are presented here.

Case 4.—A 36-year-old man was admitted to hospital Dec. 9, 1957, because of sudden onset of dyspnea and hemoptysis. In May, 1955, a mitral valvulotomy had been performed for highly symptomatic mitral stenosis. The functional result had been excellent. After this surgery, the patient had remained consistently free of signs or symptoms of cardiac failure. However, atrial fibrillation had persisted despite several conversion attempts. Because of this, digitalization had not been interrupted.

Twelve hours before admission, the patient awoke with a paroxysm of nonproductive cough. He began to sweat profusely, felt weak, and developed dyspnea and orthopnea. Coughing paroxysms continued. Three hours after the onset of symptoms, brisk hemoptysis occurred. No chest pain developed. The hemoptysis and other symptoms persisted to the time of admission.

On admission, the patient was in acute respiratory distress, coughing frequently and producing moderate amounts of bright red blood. Blood pressure level was 110/80 mm. Hg, pulse rate 110 per minute and grossly irregular, and temperature 100 F (37.7 C). Expansion of the right hemithorax appeared diminished. Coarse breath sounds and fine rales were present in the right midlung field posteriorly. Anteriorly at the right base there were scattered rales and a questionable pleural friction rub. A few rales were present in the left base. The heart was slightly enlarged to the left. The second pulmonic and first mitral sounds were accentuated. An opening snap, a soft mid-diastolic murmur, and a grade-2 blowing systolic murmur were heard at the apex. No gallop sounds were present.

Roentgenogram of the chest showed moderate cardiomegaly, accentuation of hilar vascular shadows bilaterally, and a soft infiltration extending from the hilum into the right upper lobe. The white blood cell count was 9,800 per cubic millimeter with a slight shift to the left. An electrocardiogram showed atrial fibrillation, a vertical QRS axis, and an S-T vector compatible with "subendocardial ischemia." The venous pressure was normal. Findings on blood and sputum cultures proved negative.

Oxygen therapy was started, the patient was given sedatives, and digitalization was maintained. The following morning, some 12 hours after admission, the patient appeared critically ill. The temperature had risen to 102 F (39 C), the cardiac rate averaged 110 to 120 per minute, and marked tachypnea persisted. A loud pleural friction rub was now present over the anterior aspect of the right hemithorax, and numerous rales were heard scattered throughout the right lung. The left lung was clear. Hemoptysis continued, though at a less brisk pace. Intravenous heparin therapy was begun at this time. One hour later, 75,000 FU of fibrinolysin was infused intravenously over a period of two hours.

Three hours after the start of this infusion, the patient had obviously improved. His tachypnea had subsided, and the cardiac rate had decreased to 80. The second pulmonic sound had decreased in intensity. The temperature rose to 104 F (40 C) 12 hours after infusion, then rapidly fell to normal for the first time since admission.

Twenty-four hours after infusion, an electrocardiogram showed slowing of the ventricular rate, disappearance of S-T changes, and leftward shift of the terminal QRS forces. The pleural friction rub was less striking, and the right hemithorax was moving well. Forty-eight hours after infusion, the patient was asymptomatic. The right lung was now completely clear on examination. The hemoptysis had ceased and did not recur.

Chest x-ray on the third hospital day showed decrease in the perihilar accentuation and clear lung fields. The patient was ambulated on the fourth day, and anticoagulant therapy was continued for a total of 10 days.

Case 5.—A 40-year-old woman entered the hospital because of the sudden onset of pleuritic chest pain, dyspnea, and hemoptysis. Two weeks prior to admission, the patient had had a total hysterectomy for uterine fibroids. The operation and recovery period had been uneventful, and the patient was discharged on the 10th postoperative day.

The day prior to admission, the patient suddenly developed pleuritic pain in the lateral and anterior aspects of the left hemithorax and moderate dyspnea. The pain persisted throughout the day and was still present the following morning, when the patient coughed up a small amount of bright red blood.

On her admission, blood pressure level was 120/90 mm. Hg, pulse rate 96 per minute, temperature 99 F (37.2 C), and respiratory rate 20 per minute. Dulness and a scattering of rales were present at the left lung base. The heart on examination was unremarkable, and the extremities showed no evidence of venous disease. Pelvic examination revealed some tenderness of the vaginal cuff. The electrocardiogram showed a sinus tachycardia. Chest x-ray demonstrated a zone of soft infiltration in the left lower lobe.

The patient was placed on therapy with heparin and a coumarin derivative. By the following day, she appeared improved and hemoptysis had ceased. On the third hospital day, however, the patient felt "uneasy" and had several tachypneic episodes. Examination now revealed rales at the right base, as well as at the left. The temperature rose to 100 F (37.7 C). Findings on sputum smear and culture were negative, as were those on blood culture. On her fourth hospital day, mild pleuritic pain was present on the left side and scattered rales were audible at the left base but the temperature had returned to normal. The electrocardiogram showed no alternation.

On the sixth hospital day, the patient had a sudden recurrence of pleuritic pain in the left anterior part of the chest, with renewal of dyspnea. Physical examination revealed rales throughout the lower left lobe posteriorly and a pleural rub laterally. The temperature rose to 101 F (38.3 C). The following day, the patient again had slight hemoptysis. A chest roentgenogram revealed an increase in the area of density at the left base. At this juncture, 46,000 FU of fibrinolysin was infused over a period of three hours. A temperature elevation of 1 F followed infusion. However, within 18 hours the patient's temperature had descended to 99.2 F (37.3 C). Twenty-four hours after the infusion, chest pain was absent and the patient was able to inspire deeply without pain. The pleural rub was no longer audible.

Since the recurrent embolization despite anticoagulant therapy suggested the possible necessity of inferior vena caval ligation, the patient received a second fibrinolysin infusion of 69,000 FU 36 hours after the first. Again a 1 F temperature elevation occurred. After the second fibrinolysin infusion, the patient remained free of symptoms. During the remainder of her hospital stay, she had no chest pain. Serial chest roentgenograms showed gradual resolution of the infiltration at the left base in the form of two linear scars The right base remained clear. Four days after the second infusion, the patient was ambulated and anticoagulant therapy was tapered. The patient was seen in the clinic three weeks after discharge. At that time she remained symptom-free

Peripheral Arterial Occlusion.—Experience in this study with acute peripheral arterial occlusion has been limited to three patients. One patient with embolic occlusion of the left brachial artery received fibrinolysin infusion six days after admission with no apparent benefit. Another patient with occlusion of the left radial artery secondary to trauma received fibrinolysin eight days after onset of occlusion without response. The third patient received this agent 48 hours after an embolic occlusion of the left popliteal artery. Heparin therapy and sympathetic blockade over a two-day period did not relieve the pallor, coolness, and paresthesia in the lower part of the leg. Twelve hours after fibrinolysin infusion, the temperature and color of this leg had markedly improved and paresthesia had subsided. The improvement was maintained over a four-day period of observation.

Cerebral Arterial Occlusion.—Despite multiple problems in evaluation, the paucity of effective therapeutic methods for dealing with cerebral thrombosis offers ample justification for trial of thrombolytic agents. Such therapy may be especially helpful in the syndromes of basilar or internal carotid artery insufficiency, if present concepts regarding their pathogenesis are valid.

Any criteria for differentiating thrombosis from hemorrhage are subject to considerable error. The arbitrary criteria used in this study have been (1) onset of neurological signs compatible with cerebral thrombosis without convulsion, syncope, or headache, (2) blood pressure on admission not exceeding 160 systolic and 100 mm. Hg diastolic, and (3) normal pressure, protein level, and cell count of spinal fluid.

Fourteen patients with cerebral or internal carotid artery thrombosis received infusions of fibrinolysin. In only four instances was this given within 24 hours of the onset of symptoms. In all other cases, the neurological deficit had been stable for at least three days prior to infusion. Seven patients showed some degree of objective neurological improvement (return of speech and movement) within the 24 hours after infusion. Such improvement was transient in three patients and maintained in the other four. Seven patients had no unusual degree of improvement within 24 hours after infusion.

Six patients in this group ultimately died, including three who had shown "acute improvement" and three who had not. Two of the "improved" patients died of causes other than cerebrovascular disease; the other four deaths appeared directly related to the occlusive disease. Postmortem examination was obtained in three patients. Areas of cerebral softening, without demonstrable thrombotic arterial occlusion, were found in each case. No intracerebral hemorrhages were noted.

While these few uncontrolled observations provide no basis for conclusions regarding the therapeutic value of fibrinolysin in a process as unpredictable as cerebral thrombotic disease, they do suggest the safety of such therapy. Two representative cases in which there was "acute improvement" are presented here.

Case 6.—A 51-year-old man entered the hospital on Aug. 7, 1957, for neurological evaluation. One year before admission he had had a syncopal episode. Over the succeeding months he had suffered recurrent left frontal headaches and transient ptosis of the left eyelid. Physical examination was negative, aside from indicating loss of the left corneal reflex. A carotid arteriogram on Aug. 9 demonstrated a large berry aneurysm just above the bifurcation of the left internal carotid artery.

On Aug. 14, a Selverstone clamp was applied to the left common carotid artery in the neck. Gradual occlusion was carried forward daily. By Aug. 20, the artery had been totally occluded. The patient experienced no neurological symptoms after total occlusion. On Aug. 21, the patient was taken to the operating room and the clamp removed. No pulsation was palpable beyond the site of the clamp, suggesting distal thrombotic occlusion. Ligatures were placed above and below the clamp site, and the patient was returned to the recovery room. Some 30 minutes later, the patient became unresponsive and developed a complete right-sided hemiparesis. The ligatures were immediately removed from the carotid artery. No improvement resulted, but it was noted that some pulsation was now present in the artery above the clamp site. The impression of the neurology service was that embolization had occurred from the clot in the carotid artery above the clamp, a known complication of this procedure. Lumbar puncture was negative.

The patient was placed on therapy with intravenously given heparin immediately. For the next 36 hours, the patient remained unresponsive. He exhibited marked restlessness and was incontinent. No movement returned to the right arm or leg, and speech was limited to occasional grunting. At this point, 46,000 FU of fibrinolysin was infused over a four-hour period. Heparin therapy was discontinued at this time. Seven hours after infusion, the patient was first noted to be moving the right arm and leg. His marked restlessness had subsided and bowel control had returned. He was still unable to speak but was able to understand commands for the first time since operation. At 18 hours after infusion, motion had returned to all muscle groups on the involved side save the fingers and toes, and he was able to take nourishment orally.

A second infusion of 46,000 FU was carried out 21 hours after the first. Twenty hours later, movement had returned to the fingers and toes. He ate without difficulty and attempted to talk, but could not form words accurately. Heparin therapy was now resumed.

Thereafter, his condition steadily improved. Seven days after the initial infusion, the patient was ambulatory, although the right leg was weak. The right arm and hand were weak, but the patient could employ them usefully. Over the next several weeks, a program of physical and speech therapy led to progressive improvement.

Three months after the hemiparetic incident, the patient had excellent strength in the arm and leg and had regained satisfactory speech. Further neurosurgical attack on the aneurysm was contemplated.

Case 7.—A 69-year-old man had developed a right-sided hemiparesis five years prior to admission, believed due to cerebral thrombosis, from which he had made a good functional recovery. Two days prior to admission, there was a sudden increase in right-sided weakness. The patient was unable to use the fingers of the right hand, and had poor movement at the wrist and elbow. There was also difficulty in ambulation because of marked weakness of the right toes, ankle, and knee.

Fibrinolysin infusion (46,000 FU) was carried out six hours after admission. Eighteen hours after infusion, the patient was able to clench his fist and hold objects in the hand (such as kitchen utensils, coffee cup) for the first time in three days. Ambulation was again satisfactory and ability to move the toes had returned. The improvement was maintained during 10 days of observation.

Coronary Thrombosis.—Intensive investigation in patients with coronary thrombosis has been delayed until further studies confirm that febrile responses can be prevented or adequately controlled. The present series includes only one such patient.

Case 8.—A 47-year-old man entered the hospital on Oct. 8, 1957, because of progressively more frequent, severe, and prolonged episodes of substernal chest pain. The patient had a prior history of excellent health.

Seven days before admission, while at work, he developed a "burning" abdominal pain which radiated upward beneath the sternum and was accompanied by shortness of breath. This episode subsided within five minutes. Six days before admission, three identical episodes occurred at work. The following day, while he was at home in the bath tub, pain developed which lasted 15 minutes and was associated with generalized weakness. Four days before admission, four more episodes of pain occurred, three of these while at rest. Each lasted less than five minutes. The following day, while he was resting in the evening, the patient had a very severe episode of "tight, squeezing" epigastric and substernal pain which lasted almost an hour and was accompanied by sweating, apprehension, and mild dyspnea. The patient awoke the next morning with a recurrence of identical pain, which again persisted for more than an hour. When the pain had subsided, the patient was brought to the hospital.

Physical examination on admission revealed a blood pressure level of 130/90 mm. Hg, pulse of 72 per minute, and normal temperature. The fundi were unremarkable. The lungs were clear. The heart was not enlarged, and no murmurs or abnormal sounds were present. Remainder of the examination was within normal limits.

White blood cell count, hematocrit value, and erythrocyte sedimentation rate were within normal limits. The serum amylase level was normal. The chest roentgenogram was within normal limits. An electrocardiogram showed borderline evidence of left ventricular hypertrophy and a T vector indicative of acute anterolateral myocardial ischemia.

A diagnosis of "march" angina or "impending myocardial infarction" was made, and therapy was begun with heparin and bishydroxycoumarin. He had another short episode of substernal discomfort some eight hours after entry.

Twenty-four hours after admission, the electrocardiogram was unchanged. Physical examination remained unremarkable. Temperature, white blood cell count, and sedimentation rate remained normal. The patient received a two-hour infusion of 69,000 FU of fibrinolysin. Over the next 24 hours, temperature, pulse, and blood pressure remained stable and pain did not recur.

During the third hospital day, the patient remained asymptomatic. The electrocardiogram showed definite change, with rotation of the T vector toward normal and a decrease in T-wave amplitude. On the fourth hospital day, an episode of mild substernal discomfort occurred, lasting perhaps 30 minutes. The electrocardiogram showed no change. On the fifth through the eighth day, the patient was asymptomatic, aside from a momentary "flash" of epigastric discomfort on the sixth and seventh days. Serial electrocardiograms showed a gradual return of the T vector and amplitude toward normal during this period.

The patient had no pain during the following 26 days of hospitalization. The electrocardiogram had reverted completely to normal by the ninth hospital day. At no time did fever, leukocytosis, or sedimentation rate elevation appear. During the third week a program of progressive ambulation was begun. Anticoagulant therapy was maintained throughout hospitalization and was continued on an outpatient basis. The patient has now remained asymptomatic for almost three months. His electrocardiogram continues to be within normal limits.

Superficial Thrombophlebitis.—Patients with superficial thrombophlebitis provide a valuable area for study, since this is one thrombotic state in which the thrombus can be observed directly. It is from this small group that we have derived the most objective evidence of the thrombolytic abilities of fibrinolysin.

Seven patients with superficial thrombophlebitis have received fibrinolysin intravenously. Three patients in this group had had their thrombotic process for more than seven days. In these, no beneficial effects were noted. In the other four cases, evidence suggesting thrombolysis by fibrinolysin appeared. Two of these are reported here.

CASE 9.—A 59-year-old man had had a cardiac catheterization performed via the left basilic vein on Dec. 12, 1957. The procedure was without incident. On Dec. 16, the patient complained of severe pain in the left arm. Examination revealed a palpable cord 10 cm. in length along the course of the basilic vein. This was surrounded by an area of erythema, heat, and marked tenderness. The arm was elevated and ace bandages and warm packs were applied.

Twenty-four hours later there had been no discernible improvement. Fibrinolysin (75,000 FU) was given intravenously in the opposite arm over a two-hour period. By eight hours after infusion, the erythema and heat surrounding the involved vein had decreased and the patient tolerated deep palpation of the arm with minimal discomfort. Twenty-four hours after infusion, all evidence of acute inflammation had disappeared. The venous cord was now palpable for a distance of 4 cm., representing a 6-cm. decrease in length since infusion. Minimal tenderness to palpation remained over the distal part of this cord. The patient could use the arm without discomfort.

All tenderness over the vein had subsided by the fourth day. Observation for eight days after infusion showed no return of symptoms or signs. A 4-cm. zone of clot still remained palpable at the end of this period.

CASE 10.—A 56-year-old man was referred to me because of multiple painful thromboses in the superficial veins of both arms. During two prior weeks of hospitalization various diagnostic and therapeutic procedures had required numerous venipunctures, many of which had been followed by development of local superficial phlebitis. At the time of examination, two areas of active phlebitis were present. A thrombosed segment of vein some 5 cm. long over the right forearm had followed a venipuncture 48 hours prior. In the right antecubital area, a thrombosed segment measuring 3.5 cm. had followed a venipuncture 24 hours prior. Both thrombi were paralleled by an area of erythema, heat, and tenderness which extended above and below them for a short distance. Six other areas of venous thrombosis were present in the forearms and antecubital fossae. These showed no evidence of inflammation, ranged from 2 to 5 cm. in length, and were one to two weeks old.

Fibrinolysin (46,000 FU) was infused via an uninvolved vein in the right forearm. Twenty-four hours after infusion, the two "active" areas no longer showed evidence of inflammation. The palpable thrombus in each had disappeared, and blood could be withdrawn easily from both. The other zones of palpable thrombus showed no change. Improvement in the areas mentioned was maintained over an observation period of six days. Hematological evaluation of this patient disclosed no cause for his "thrombotic tendency" to venipuncture.

Comment

The availability of an agent of low toxicity which is capable of acutely dissolving intravascular clot would represent a major advance in the therapy of thromboembolic disease. On the basis of the studies reported above, one is justified in cautiously suggesting that fibrinolysin (plasmin) may be such an agent.

Promising qualities of fibrinolysin demonstrated by these investigations include the following observations: 1. The ability of the material to produce an active intravascular fibrinolytic system in the majority of patients. At the higher dosage levels, significant plasma fibrinolytic activity is frequently maintained for at least 24 hours. 2. The low toxicity of fibrinolysin infusion, which is limited primarily to pyrogenicity at the dosages employed. Hemorrhagic complications have not occurred. Anticoagulant drugs can be safely used simultaneously. Laboratory studies indicate that a wide margin of safety exists between fibrinolysin dosages which can enhance plasma fibrinolytic activity and those which may impair coagulation. Embolization has not complicated the therapy of venous thrombotic disease. Allergic reactions have been rare and mild. 3. The clinical results after fibrinolysin infusion, which have been consistently encouraging in terms of its apparent ability to dissolve a recently acquired intravascular clot.

These observations constitute an impressive array of "plus signs" on the fibrinolysin balance sheet. However, at least four major facets of fibrinolysin therapy appear to require further study: (1) certain aspects of fibrinolysin toxicity; (2) establishment of proper dosage schedules; (3) accurate estimation of the value of fibrinolysin in various thromboembolic states; and (4) the need for anticoagulant therapy after acute thrombolysis.

Toxicity.—The problems of toxicity, at the dosages used in this study, appear restricted primarily to elucidation of the cause of the febrile reaction to fibrinolysin. Present data indicate that profibrinolysin is not pyrogenic. Since no streptokinase activity can be demonstrated in the fibrinolysin material itself, streptokinase cannot be incriminated. Therefore, fever must stem from either pyrogenic, nonstreptokinase residuals of the activation process or from the actions of fibrinolysin itself within the body. The more frequent occurrence of fever in patients with extensive thrombotic zones suggests that febrile reactions may result from the protein fractions released when fibrinolysin acts upon fibrin. Whatever its cause, the danger of pyrogenicity presently limits the application of this material in such critical states as coronary thrombosis. Further study regarding its etiology and the ability of aspirin-antihistaminic prophylaxis to control fever is therefore of considerable importance.

While minimal toxicity followed fibrinolysin infusion in this study, it is important to recognize that the observations regarding toxicity did not extend beyond doses of 90,000 FU. Significant depletion of coagulation factors, and perhaps other toxic effects, may occur at higher dosage levels. Since fibrinogen appears to be the most sensitive of the clotting factors to fibrinolysin infusion, qualitative measurement of fibrinogen before and after infusion would enhance the safety of fibrinolysin therapy. Presently, such measurement appears mandatory if dosages above 90,000 FU are employed.

Proper Dosage Schedules.—Determination of the ideal fibrinolysin dosage in various thrombotic states will require systematic study of large patient groups. The present investigations have indicated that considerable plasma fibrinolytic activity can be maintained for 24 hours in patients receiving 69,000 units or above. However, it is not known whether demonstrable plasma fibrinolytic activity must be achieved and maintained to bring about the dissolution of intravascular clot. In view of the strong adsorptive capacity of fibrin for fibrinolysin,[10] it is quite possible that fibrinolysin may exert considerable local effect upon a clot in the absence of demonstrable plasma fibrinolytic activity. Therefore, small, repeated doses of fibrinolysin may prove as efficacious as single, larger infusions.

It is equally possible that local factors may prevent access of fibrinolysin to a clot in some cases and lead to therapeutic failure, even in the presence of marked plasma fibrinolytic activity. Therefore, dosage of fibrinolysin will remain largely empirical until further experience permits adequate correlation between clinical effect and level of plasma fibrinolytic activity.

Therapeutic Value of Fibrinolysin.—Accurate estimation of the therapeutic value of fibrinolysin in various thromboembolic disorders poses a challenge of considerable magnitude. The complexity of such evaluation stems from our present inability to define with certainty the pathogenesis, diagnosis, and prognosis of most forms of vascular occlusion. For example, the consequences of coronary occlusion are identical whether the pathogenic basis for occlusion is thrombosis, subintimal hemorrhage, or embolization of atheromatous material. Obviously, fibrinolysin could not be expected to restore vascular continuity if either of the latter two mechanisms are operative. In cerebrovascular insults, the pathogenic possibilities are even greater.

Regarding diagnostic uncertainty, the problems involved in the precise diagnosis of pulmonary embolism or deep venous thrombosis are widely appreciated. The same lack of precision applies to prognosis, for thrombotic states are notoriously capricious in their "natural course." Such variability demands that considerable caution be exercised in attributing improvement to any therapeutic agent. The problem of prognosis is further complicated by the fact that there may be wide variation in the degree of functional return which can be expected in tissues sensitive to short periods of nutrient lack, even if thrombotic occlusion is totally relieved.

These multiple problems are not new. The complexities of evaluating agents used in thromboembolic disorders are vividly in evidence today in the form of the controversy which still rages regarding the value of the anticoagulant drugs in many conditions. As with the anticoagulant drugs, reliable evidence regarding the therapeutic value of fibrinolysin in most forms of thromboembolism will require large, controlled series. However, it should be recognized that "controlled" fibrinolysin series will not be valid unless attention is paid to another critical variable; namely, the age of the thrombotic process. In animal studies,[13] Cliffton and Ambrus have found that fibrinolysin is highly successful in dissolving intravascular clot as long as three days after formation. Beyond this point, experimental thrombi appear relatively resistant to fibrinolysin. Since animal studies involve artificial situations in which considerable vessel-wall trauma accompanies thrombosis, it is questionable whether such data can be applied directly to human thrombotic disease. However, it is clear that fibrinolysin "success" or "failure" will have to be interpreted with due regard to the probable structure of a clot at the time thrombolysis is attempted.

Need for Anticoagulant Therapy After Acute Thrombolysis.—Animal studies have suggested that rethrombosis after successful clot dissolution may occur when fibrinolysin is used alone but can be prevented when heparin is used concurrently.[12] Therefore, it appears that anticoagulant drugs should be used to avoid rethrombosis in all patients, unless circumstances clearly indicate that the factors which led to thrombosis have subsided.

This discussion has made it plain that the therapeutic evaluation of fibrinolysin will not be a simple task. While the results of these preliminary studies provide a firm basis for optimism regarding fibrinolysin, excessive enthusiasm should be avoided until further investigation has been completed. If the fibrinolytic agents are to be employed with maximum safety and benefit, therapeutic impatience must be tempered by sufficient scientific skepticism to delay widespread employment of these agents until an instructive body of controlled data can be accumulated.

Summary

A pilot study of the effects of intravenously given fibrinolysin (plasmin) has been carried out in 52 patients with various forms of thromboembolic disease. Toxicity, fibrinolytic activity achieved in the plasma, and therapeutic results were carefully evaluated.

In the doses used, toxicity of the agent appears limited to pyrogenicity, which was encountered in 49.2% of the patients. The mechanism of this response has not been defined. Two instances of delayed allergic skin reactions were noted. No embolic events have followed fibrinolysin infusion. Serial study of coagulation factors after infusion of fibrinolysin showed no clinically significant derangement of the coagulative process. No hemorrhagic phenomena were encountered in any patient, including 29 who were simultaneously receiving anticoagulant drugs.

Fibrinolytic activity of the plasma was consistently enhanced by fibrinolysin infusion. The intensity and duration of such activity paralleled total fibrinolysin dosage.

While the therapeutic results observed after infusion of fibrinolysin in several varieties of thromboembolic disease were encouraging, firm conclusions regarding its therapeutic value cannot be drawn from this pilot study and must await completion of large-scale controlled studies. However, the observations reported here do justify a cautious optimism that fibrinolysin may prove a safe and effective agent for achieving acute lysis of intravascular clot.

District of Columbia General Hospital, 19th and E streets S. E. (3).

The fibrinolysin used in this study was supplied as Actase by the Ortho Research Foundation, Raritan, N. J.

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SCHOOL HEALTH.—One of the first things that will bring about a mutual understanding between school health and public health is a policy on communicable disease control. A complete and satisfactory agreement can be made with regard to local control of communicable diseases in a joint meeting with the school health committee of the County Medical Society, local health officers and the director of school health. . . . In planning a health education program, public schools and public health agencies should join with other agencies and make it a community project. A community health council organized by all official and non-official agencies in the community may serve as a clearing-house for all community health education program planning. Newer methods of health education can be developed and put into action when the community agencies work together.—A. E. Hill, M.D., M.P.H., Correlation Between School Health and Public Health, *The Journal of School Health,* May, 1958.

THROMBOLYSIS WITH FIBRINOLYSIN IN CEREBRAL ARTERIAL OCCLUSION

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Three patients with hemiplegia were treated by the slow intravenous infusion of fibrinolysin. The site of occlusion of the cerebral vessels was located in each case by arteriography. In one case the angiograms clearly showed nonfilling of the middle cerebral group of arteries before treatment, while on the eighth day after beginning treatment good filling of the middle cerebral vessels was obtained. This patient showed the most favorable results. The history of rheumatic heart disease and the fact that treatment was commenced within six hours after the onset of symptoms suggest that the lesion was caused by an embolus originating in the fibrillating left atrium and that the embolus was a fresh thrombus most susceptible to the lytic agent. No detrimental effects that could be ascribed either to the diagnostic angiography or to the administration of fibrinolysin were observed in these patients.

The most promising therapy for thrombotic occlusion of any vessel supplying the brain will probably be immediate solution of the clot by a parenterally administered agent. A surgically directed approach to the problem may be frustrated by the increasingly apparent complexities of vascular thrombosis. The appearance of symptoms may depend on complicated relationships between anastomotic channels. There is increasing evidence to make us speculate that a hemiplegia resulting from an apparent angiographically demonstrated thrombosis of the carotid artery, or of its cerebral branches, may actually result from the final thrombotic closure or stenosis of a vital collateral vessel elsewhere that is compensating for a long-standing obliterated proximal channel. Although transient neurological deficits may be related to alterations of the general systemic blood pressure, on which the stability of the collateral circulation depends, the more persistent and complete deficits are more likely the result of a final strategic thrombosis or other form of occlusion. Whatever might be done by the surgeon electively for lesser symptoms when the site of thrombosis or stenosis is demonstrable, in the presence of a severe neurological deficit, only the immediate elimination of the thrombus is likely to be of benefit. It is not believed practical that this can be accomplished surgically in the majority of instances.

There have been many reports in recent years of angiographically proved cases of carotid or major cerebral artery thrombosis.[1] Several workers have undertaken a surgical approach to the problem. Strully and associates[2] performed an incomplete thromboendarterectomy in 1953 in a patient with signs of aphasia and visual disturbance. They speculated that, under more favorable circumstances, the procedure might be effective. We have recently observed such a satisfactory complete removal of the thrombus within 24 hours of the appearance of hemiplegia and aphasia. Although vigorous flow was at least temporarily reestablished, the patient obtained no improvement. We have witnessed marked improvement after carotid thromboendarterectomy in a case of partial aphasia and hemiparesis; however, we cannot be certain that the surgery was responsible. Arnstein[3] is more enthusiastic about this procedure, although only 2 of his 10 patients would appear to have been radically improved after total deficit. Eastcott and associates,[4] Lin and co-workers,[5] Denman and associates,[6] and others have attempted to remedy either minor or recurrent episodes of neurological deficit by various other techniques, generally consisting of a vascular bridging graft or resection of the diseased arterial carotid segment. Although some improvement has been obtained under these circumstances, there has not yet been reported a patient with hemiplegia or global deficit who has made dramatic recovery after one of these procedures. Some lesser degree of recovery is to be expected without intervention. In this respect, Jackson[7] has recently demonstrated how, in two cases of improvement, the supposedly restored channel was proved to be obliterated at reexploration or angiography. In addition, surgery may actually interfere with the collateral if, unwittingly, the external carotid artery is kept from its function of supplying flow via the ophthalmic artery to the carotid, as shown by Vaernet.[8]

It is our feeling that the results of these procedures are not very encouraging, particularly under the circumstances of global deficit. With minor deficits or recurrent episodes, it is very likely

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that, in conjunction with anticoagulants, they offer some therapeutic and prophylactic promise. In the severe cases, the principal handicap inherent in this technique is the poorly tolerated delay between the appearance of symptoms and the removal of the thrombus. As demonstrated by Denny-Brown and Meyer,[9] this critical period must be very short before the changes in the damaged area of the brain become irreversible. This time is ordinarily consumed in the obligatory delay required for consultation between family physician and specialist, transportation, diagnostic angiography, and preparation for surgery. What has been needed is an agent, known to be effective in reversing thrombosis, which can be administered immediately on the appearance of symptoms by the first physician to arrive on the scene. Needless to say, the applicability of such a drug in the smaller vessel thromboses is enormous. It is hoped that in this study, in which the enzyme fibrinolysin has been used, there may be some promise of such an agent.

Fibrinolysin (plasmin)[10] is a naturally occurring proteolytic enzyme of plasma. Purified human plasminogen or profibrinolysin, its precursor, may be spontaneously activated in vivo to fibrinolysin or in vitro by urokinase (an enzyme obtained from urine). The effect of fibrinolysin, as demonstrated by many workers,[11] is the dissolution of vascular thrombi. This drug has been used clinically in the three patients reported here. Particular attention is invited to the third case.

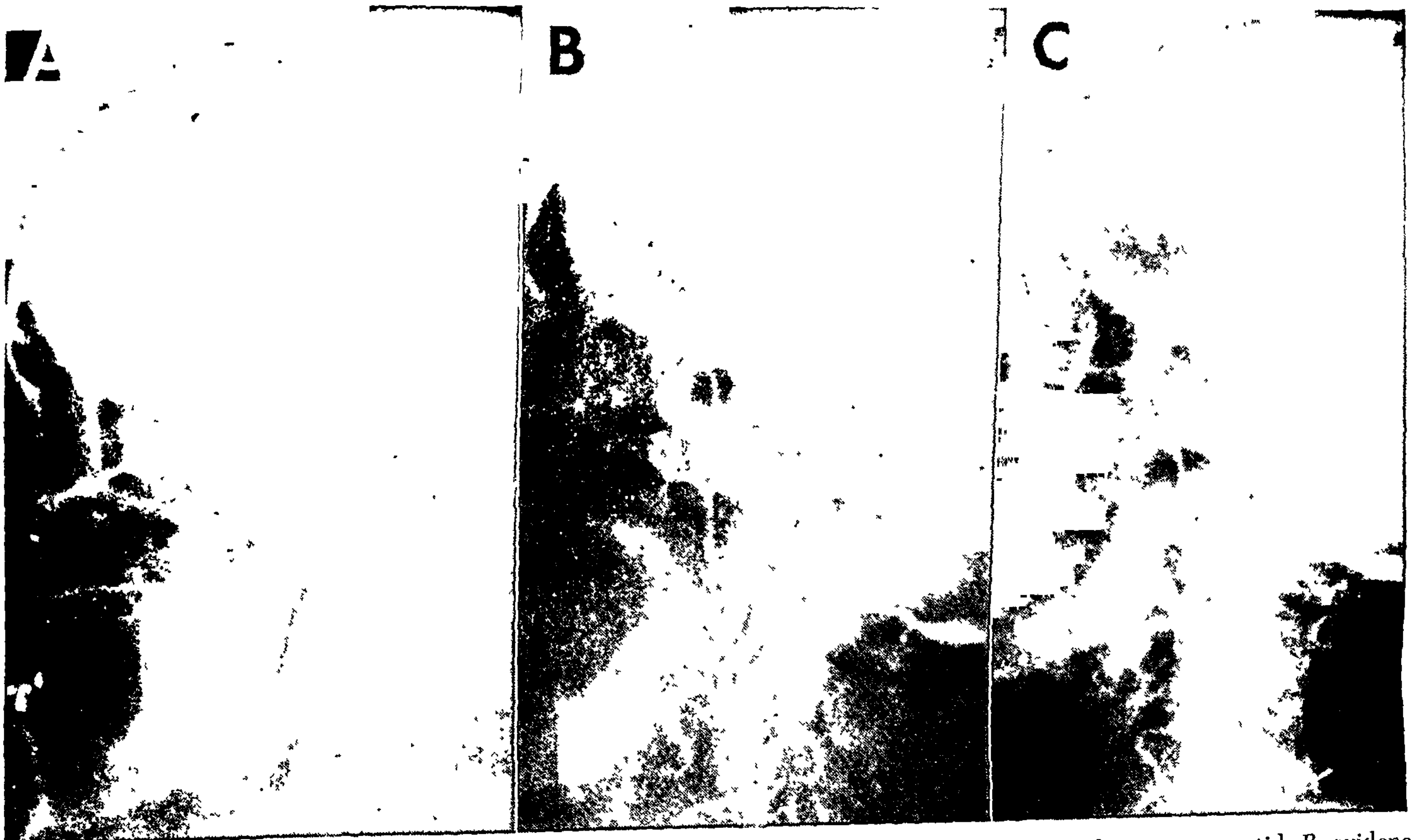

Fig. 1 (case 1).—*A*, arteriogram showing thrombosis of internal carotid artery at bifurcation of common carotid. *B*, evidence of partial clearing of internal carotid after six days of therapy. *C*, slight further clearing after six additional days of therapy.

Report of Cases

Case 1.—A 75-year-old woman, right-handed, was admitted to the hospital on Sept. 6, 1957, because of the abrupt appearance of hemiplegia of the right side and inability to speak. She was known to have hypertension of many years' duration and had required recent treatment for dyspnea and cystitis.

Physical Examination.—The patient aroused easily but could not speak and did not comprehend. A complete spastic hemiplegia on the right side was evident, with increased deep tendon reflexes and ipsilateral Babinski's signs. There was a moderate supranuclear facial weakness on the right. A resting alternating tremor of the left hand and forearm was observed. The carotid pulsations on the left varied on repeated examinations. Cardiac enlargement and a systolic apical murmur were noted. The blood pressure was 180/90 mm. Hg.

Laboratory Data.—The blood cell count was normal. Urinalysis revealed 1+ albumin, 6-10 white blood cells, 80-120 red blood cells, and bacteria. A left carotid arteriogram performed on Sept. 12, 1957, demonstrated nonfilling of the internal carotid artery beyond the bifurcation of the common carotid (fig. 1*A*).

Course.—On the same day, 50,000 units of fibrinolysin was given intravenously in 300 cc. of isotonic sodium chloride solution over a three-hour period. Simultaneously, 25,000 units in 100 cc. was given after one hour, over a 15-minute period, into the left carotid artery. This was repeated on three of the next four days. One injection of 200 mg. of heparin was administered on the day no fibrinolysin was given. A second left carotid arteriogram taken on Sept. 16, 1957, showed an incomplete 2-cm. column of dye in the proximal internal carotid (fig. 1*B*). Accordingly, 75,000 units of fibrinolysin was given daily, intravenously, in 500 cc. of isotonic sodium chloride solution over a two-hour period for the following six days. On Sept. 24, 1957, another left carotid arteriogram showed slight further change (fig. 1*C*). No hypotensive effects of the drug were observed in this patient. There was some elevation of temperature, which ranged between 101 and 102 F (38.3 and 38.7 C), but this may have been due to chronic cystitis. The patient showed no improvement of her hemiplegia or aphasia. She appeared more alert, however, and was able to take oral feedings better after the course of treatment.

Case 2.—A 52-year-old right-handed man was admitted to the hospital on Sept. 28, 1957, because of progressive hemiparesis of the left side. About one hour prior to admission, he noted weakness of the left lower extremity, which rapidly became complete. He had been in good health prior to this illness.

Physical Examination.—The patient was alert but somewhat facetious. There was a complete, slightly spastic paralysis of the left lower extremity. The left upper extremity was weak and much more spastic than the lower, with most involvement proximally. The deep tendon reflexes were hyperactive on the left. A Babinski's plantar reflex was obtained on the left. Findings in the general physical examination were within normal limits. The blood pressure was 130/80 mm. Hg, and the pulse rate was 90 per minute and regular.

Laboratory Data.—Blood cell count and findings on urinalysis were normal. A right carotid arteriogram performed six hours after admission demonstrated occlusion of the anterior cerebral artery at the point of bifurcation into the pericallosal and callosomarginal vessels (fig. 2).

Course.—Immediately after angiography, the patient received, intravenously, 100,000 units of fibrinolysin in 50 cc. of isotonic sodium chloride solution over a two-minute period. On each of the following five days, an infusion of 100,000 units was given in 500 cc. over a two-hour period. On Oct. 3, 1957, angiography failed to reveal any further filling of the anterior cerebral artery. During this period, a progression to a complete hemiplegia of the left side was noted. This was associated with a tendency to ignore the paralyzed limb and a mild hypalgesia over the left side of the body, as well as defective proprioception. These sensory findings gradually disappeared as the patient became aware of his deficit. In addition, there was noted a disappearance of the spasticity of the left upper extremity and an occasional demonstration of ability to extend the left lower extremity when supported by the examiner. During the course of therapy, a sustained temperature elevation of 102 to 103 F (38.7 to 39.4 C) was observed. This reverted to normal after cessation of the enzyme administration. A solitary hypotensive episode with a blood pressure reading of 90/40 mm. Hg was seen on the fifth day of treatment.

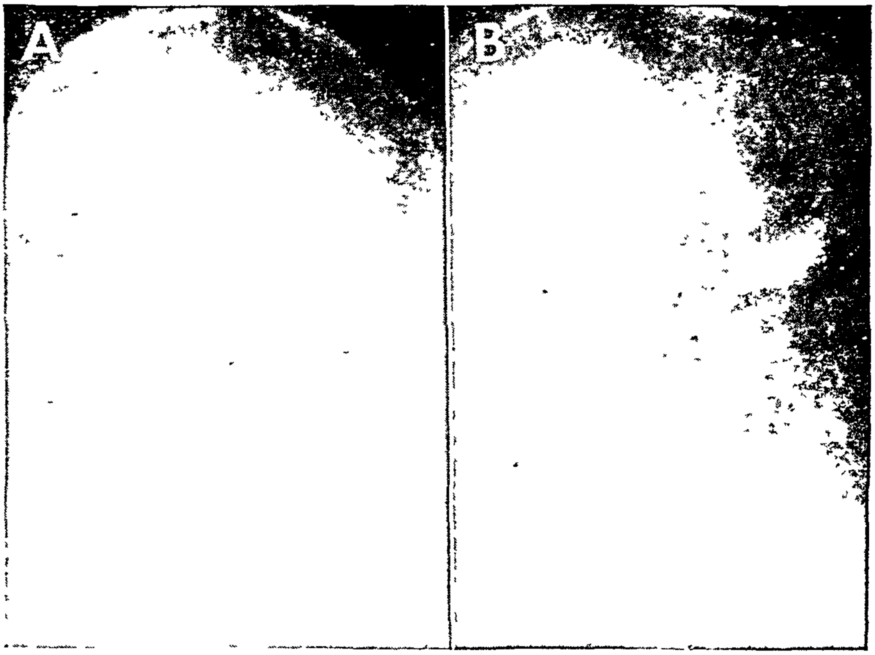

Fig. 2 (case 2).—*A*, anteroposterior arteriogram, showing occlusion of the anterior cerebral artery immediately beyond the frontopolar branch and nonvisualization of the pericallosal and callosomarginal vessels. *B*, lateral arteriogram, with only the main trunk and frontopolar and prefrontal branches of the anterior cerebral artery seen. Vessel is seen to truncate abruptly at point of occlusion immediately beyond frontopolar origin.

Case 3.—The patient, a 50-year-old right-handed woman, was admitted to the hospital on Oct. 22, 1957, after falling from bed on attempting to arise that morning. A paralysis of her left upper and lower extremities was noted. There was a long history of rheumatic heart disease, with fibrillation; this had been treated by digitalization and diuretics for five years. Chronic ascites was noted to have increased during the week prior to admission.

Physical Examination.—The patient was disoriented and confused. There was a complete flaccid hemiplegia on the left side, with ipsilateral increased deep tendon reflexes and Babinski's plantar reflex. A supranuclear facial weakness was noted on the left. In addition, a left homonymous hemianopsia and hemisensory disturbances were found. The heart was enlarged, with distant sounds and a grossly irregular pulse rate. The abdomen was markedly distended by ascitic fluid. Blood pressure measured 116/80 mm. Hg, and pulse rate was 60 per minute and irregular.

Laboratory Data.—The blood cell count and findings on urinalysis were within normal limits. An electrocardiogram showed auricular fibrillation, with slow ventricular rate, right axis deviation, and low-voltage QRS complexes. Angiography demonstrated nonfilling of the middle cerebral group of vessels (fig. 3*A*).

Course.—The patient was immediately administered 100,000 units of fibrinolysin in 50 cc. of isotonic sodium chloride solution, intravenously. On the six successive days she received the same amount of enzyme in 200 cc. of solution, by infusion, over a one-hour period. The temperature was elevated to 101 F (38.3 C), with daily spikes ranging from 103 to 105 F (39.4 to 40.5 C). There were a few hypotensive phenomena, with occasional blood pressure readings of 100/60 mm. Hg. During the last five days of treatment, the patient could occasionally extend the left lower extremity at the knee. On the eighth day, a repeat carotid arteriogram revealed good filling of the middle cerebral group (fig. 3 *B*).

Comment

The primary problem in this group of cases was the uncertain nature of the occluding lesion. In the third patient, in whom the most gratifying results were obtained, it is assumed that the source of obstruction was an embolus originating in the fibrillating auricle. She was treated, after study, within six hours of the appearance of symptoms. There was some speculation while this patient was under treatment whether the composition of the embolus might be older than the short clinical course suggested. It is believed, however, that the lodging embolus actually was the released fragment of a fresh thrombus. It is this type of fresh clot that is probably most susceptible to the lytic agent. The arteriograms suggest that, in this case, a restitution of the sylvian artery circulation was accomplished. The first patient treated was not seen until a week after the onset of symptoms. It is not believed that a thrombus of this age is a satisfactory substrate for the digestive action of the enzyme, although some lytic action was demonstrated in this case. The possibilities of a subintimal dissection of the wall underneath an atherosclerotic plaque or a progressive sclerosis are further situations in which it is not reasonable to expect drug action. It is possible that one of these factors accounted for the failure in the second patient. In the large group of cases, however, where a fresh thrombus is the final source of occlusion, it is believed that the drug may be effective if administered promptly.

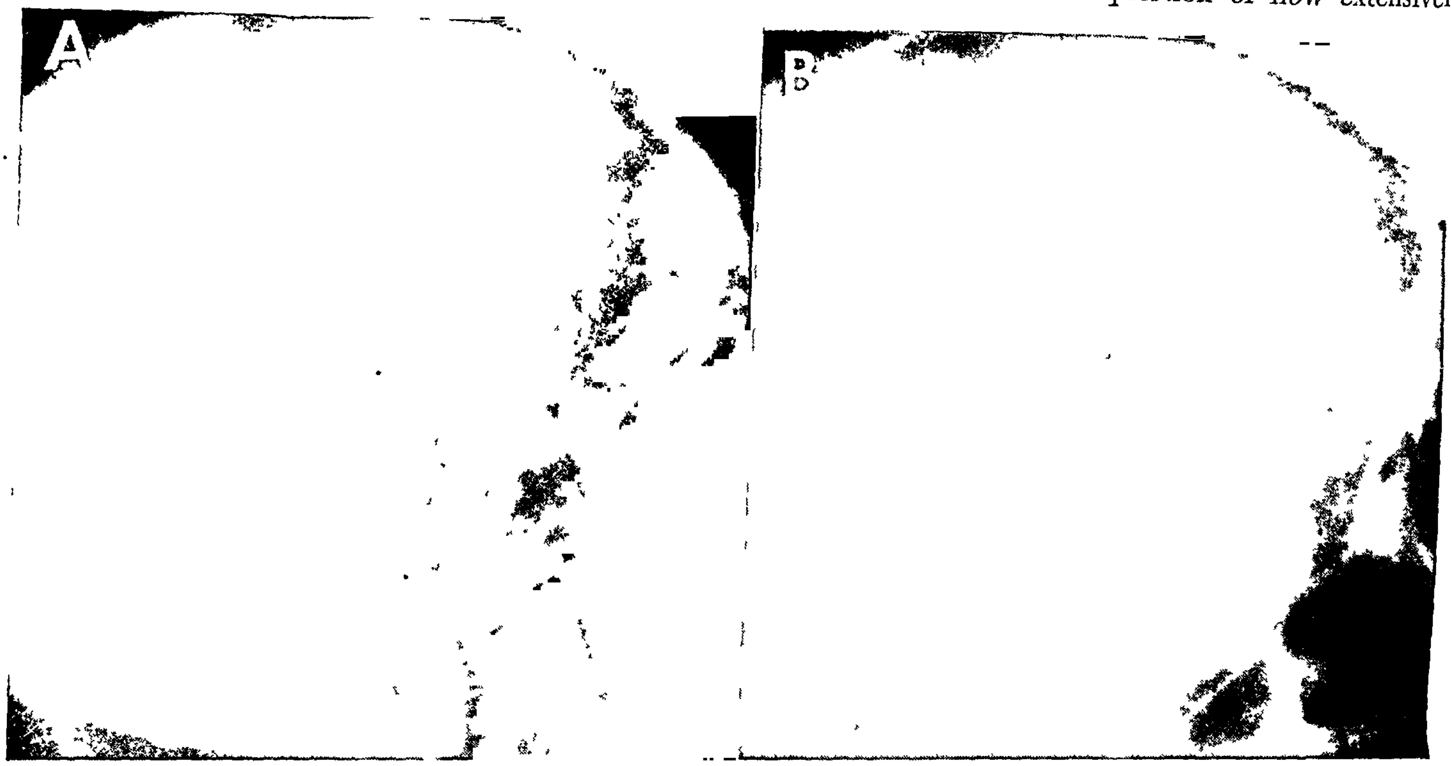

Fig. 3 (case 3).—*A*, arteriogram showing occlusion of middle cerebral artery at origin from carotid. Only anterior cerebral, posterior communicating, anterior choroidal, and posterior cerebral branches of carotid are seen. *B*, good visualization of sylvian artery group, except for ascending frontal branches, seven days after treatment.

Studies of the blood levels of the enzyme were conducted on all three patients. The use of the drug has been implemented on an empirical basis. It is not certain what constitutes a satisfactory therapeutic dose or course of treatment. We do not know how soon the thrombus may be expected to dissolve. The possibility of greater advantage to be obtained from intracarotid administration has been considered. Some preliminary work along this line was carried out on the first patient. Further studies are being conducted.

There was observed a consistent pyrogenic effect of the drug, as well as some mild hypotensive episodes in two patients. These side-actions were not deleterious in these cases and did not require treatment. We have encountered no evident complications of fibrinolysin administration.

It is of clinical interest that the patient with anterior cerebral artery occlusion developed a complete hemiplegia, with transient sensory deficits. In characteristic fashion, the lower limb was involved first, with associated proximal upper limb weakness that spared the hand. The complete paralysis that followed, however, showed signs of improvement in the lower limb alone. This provocative correlation raises anew the question of how extensively the motor cortex may be represented along the medial surface of the hemisphere. In addition, it is further evident that our clinical localization of the site of thrombosis may be very subject to error.

There were no untoward reactions to angiography in this group of patients. Although we are not enthusiastic about the repeated performance of arteriography in patients with cerebrovascular disease, we have not observed complications in this group or in another previously reported.[14] There is, unfortunately, no alternative to arteriography before and after treatment. Clinical improvement is a poor indicator of efficacy, for this usually occurs to some degree in most cases of cerebral thrombosis.

Summary

In a preliminary study, three patients with occlusive carotid or cerebral vascular disease were treated with fibrinolysin. Arteriography demonstrated the site of obstruction in all three cases. Restitution of the middle cerebral artery circulation was observed in one patient. In a second, partial clearing of an occluded carotid lumen was observed. The other patient showed no alteration of his anterior cerebral artery occlusion. We are impressed with the possible advantageous action of fibrinolysin. It is believed that its prompt administration in cases of cerebral thrombosis or embolism may prove beneficial. It is not expected to benefit patients with progressive atherosclerotic occlusion in whom an actual thrombus does not occlude the lumen. Its specific usefulness in treatment of embolism has been suggested by the results obtained in one patient. Further studies are being carried out.

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The fibrinolysin used in this study was supplied as Actase by the Ortho Research Foundation, Raritan, N. J.

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CHRONIC CONSTRICTIVE PERICARDITIS.—In the 21 years from 1935 through 1955, 72 patients have undergone operation for constrictive pericarditis at the clinic. Follow up data were available for periods varying from three months to 17 years from examination at the clinic or from follow up letters. There were 49 males and 23 females in this series, and the majority were from ten to 39 years old. Many disease entities have been considered precursors of chronic constrictive pericarditis. The great majority of these cases, however, were not associated with any condition which might be blamed etiologically. Only 19 of the 72 patients gave a history of any previous infection or incident which conceivably might have been related to the development of constrictive pericarditis. Eleven afforded microscopic evidence of granulomatous pericariditis compatible with tuberculosis. In only six of the 11, however, could tubercle bacilli be isolated by culture. In 59 instances the pathologist diagnosed chronic nonspecific pericarditis, and in two additional cases both acute and chronic pericarditis of a nonspecific variety were present; but no single factor or group of them was found consistently to account for the onset of constrictive pericarditis.—J. C. Cooley, M.D.; O. T. Clagett, M.D.; and J. W. Kirklin, M.D., Surgical Aspects of Chronic Constrictive Pericarditis, *Annals of Surgery*, April, 1958.

J.A.M.A., Aug. 2, 1958

ADJUVANT USE OF CHEMOTHERAPY IN THE SURGICAL TREATMENT OF CANCER

PLAN OF COOPERATIVE STUDY

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A plan is described for the cooperation of 48 departments of surgery under the auspices of the National Cancer Institute in a study of the effectiveness of chemotherapy as an adjuvant to the surgical treatment of cancer. It has three aims: to improve the prognosis of the patient with cancer, to determine whether certain chemical agents are curative, and to develop workable techniques for therapeutic trials. Two investigations specifically planned relate to the use of Thio-TEPA (triethylenethiophosphoramide) in resectable gastric carcinoma and of nitrogen mustard in resectable pulmonary carcinoma. The results of animal research encourage such work, since small tumors have been found more susceptible than larger ones to regression, and the probability of metastasis is less when the number of neoplastic cells in the primary tumor is small. The plan includes the use of standard criteria of diagnosis, treatment, and measurement of effect; the pooling of data from all collaborating institutions; and the participation of statisticians in designing the study and evaluating the results.

This report presents some of the background and the study plan of a large national endeavor in clinical research on cancer that has been developed under the auspices of the Cancer Chemotherapy National Service Center of the National Cancer Institute. The study is known as the Adjuvant Use of Chemotherapy in the Surgical Treatment of Cancer, and its major purpose is to assess the effect of known anticancer chemical agents when administered in conjunction with definitive treatment of cancer at a stage when the neoplasm may be clinically curable.✓The aims of the study are threefold: (1) to establish whether this additional measure will yield improvement in the end-results, (2) to ascertain whether some of the presently available anticancer agents which have had only a palliative effect against established neoplasms may have a curative effect in earlier stages of cancer, and (3) to develop methods and techniques for clinical therapeutic trials in cancer.

The participation of 48 departments of surgery in these studies and the approval and support of this research by the National Advisory Cancer Council are the results of gradual changes in concepts regarding cancer. These concepts have led to the realization of the limitations of surgical and radiologic treatment of cancer that attempts to circumscribe and to remove the neoplasm and to the realization of the possibility of discovering effective chemical agents against cancer.

The First Aim

The first aim of these clinical studies is directly therapeutic: to improve the prognosis of the patient with cancer. It is possible to record steady albeit slow improvement in the end-results of the treatment of cancer in the United States.[1] The basic problem of the excisional approach to cancer, however, is that a majority of patients in whom the local disease has been eradicated die from the distant spread of cancer cells through lymphatics, vascular channels, and body cavities.

Research work on animals has demonstrated that very early spread of tumor cells can occur to sites distant from implanted tumors but that a relatively small proportion of such cells gives rise to eventual metastatic growth.[2] Although the transplantation of leukemia and some sarcomas in mice can be accomplished by inoculation with a single neoplastic cell,[3] successful transplantation of most tumors requires rather large numbers of tumor cells.[4]

It seems likely that similar factors may be involved in man during the transplantation process of metastasis. Smith and his co-workers [5] recently have reported on the recovery of tumor cells from the washings of operative wounds for cancer. The most interesting finding was that almost half of the patients in whom such tumor cells were identified did not develop local recurrence.

In chemotherapeutic research on animals with transplanted neoplasms, it has been the practice to use tumors after they have become well established and are actively growing in the new host. It is known that, during the earlier stages of tumor growth, conditions between the tumor and the host are different from conditions at later stages and that small tumors appear to be more

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susceptible to regression than larger ones. The interrelationships between tumor, host, and drug recently have been reviewed by Goldin.[6]

Recent experimental work further substantiating that earlier, unestablished tumor foci are more susceptible to destruction than established, larger tumors has been published by Goldie and associates,[7] who used radioisotopic materials, and by Cruz and associates,[8] Kramer and associates,[9] and by Lapis and Németh,[10] who used alkylating chemicals. The intricate mechanisms that may be involved are suggested by the finding of Kramer and associates[9] that Thio-TEPA (triethylenethiophosphoramide) is more effective in preventing pulmonary growth of melanoma S-91 in mice when it is given one or two days after tumor cell inoculation than when it is given immediately after the intravenous transplantation. Shapiro and Fugmann[11] reported an experiment in mice bearing carcinoma 755, in which four groups of animals were treated as follows: (1) with no surgery or chemotherapy, (2) with chemotherapy only, (3) with surgical excision only, and (4) with subtotal surgical excision and chemotherapy. In this particular system there were no survivors among the first three groups, whereas half of the mice in the fourth group became free of tumor.

In most of the studies mentioned above, the investigators used a tumor which was sensitive to the particular chemical agent. Furthermore, all of the tumors were transplants, and thus some host reactions can be assumed. When relatively unresponsive tumor-agent combinations are used, the chemotherapeutic action upon even unestablished tumor cells may be negligible.

If toxic chemotherapeutic compounds do not destroy the cancer cells and do decrease the host's resistance, an adverse effect on the host may occur. Many investigators have noted that cortisone reduces host resistance, with resultant acceleration of tumor implantation and growth. Kondo and Tsukui[12] demonstrated this phenomenon by treating animals with Nitromin (2,2′-dichloro-N-methyldiethylamine N-oxide hydrochloride) before inoculation of tumor cells. Personal experience suggests that enhanced growth of advanced neoplasms in patients may take place if an ineffective toxic anticancer agent is used.

There have been several clinical studies in which chemical or radioisotopic agents were used in conjunction with the surgical treatment of cancer. These investigations are distinctly different in approach from the earlier combinations of radiation and surgery, where essentially an enhanced local or regional effect was the intent.

Low-Beer and Bell[13] administered radiophosphorus in conjunction with radical mastectomy for breast cancer; the authors previously found some differential absorption of radiophosphorus by breast tumors. Cole and his colleagues[14] deserve credit for initiating and developing interest in the United States in the use of nitrogen mustard and Thio-TEPA at the time of surgical resection of gastrointestinal neoplasms. It is reported from Japan[15] that Nitromin is being used after surgical treatment of a wide variety of neoplasms. In Germany and Austria[16] both Nitromin and E-39 [2,5-bis-(ethylenimino)-3,6-dipropoxy-*p*-benzoquinone] are being explored as adjuvants to surgery. None of these studies has as yet provided definite answers regarding the effects of adjuvant therapy.

The Second Aim

The second aim of the studies is a corollary of the first: to determine whether certain chemical agents are curative in human cancer. The modern era of research in the chemotherapy of cancer began under the cloak of wartime secrecy, with the discovery of the antineoplastic activity of nitrogen mustard by Gilman and Philips. By 1948 there had appeared the work on antifolic compounds by SubbaRow and their clinical application by Farber and on urethane and the alkylating agents by Haddow and his group. The work in this exciting field, still in its infancy, has been summarized recently by Farber and associates.[17] Except for the effect of antifolic compounds and 6-mercaptopurine in childhood leukemia, no significant prolongation of life can be demonstrated with the use of chemical agents in advanced neoplastic disease in man. Yet some of these compounds are sufficiently active to cure certain established transplantable neoplasms in rodents. It would certainly be useful and encouraging to the further development of this line of research if it could be demonstrated that chemotherapeutic agents for cancer already available have curative activity under more favorable circumstances than those presented by patients with neoplasms no longer amenable to any other therapeutic approach.

This possibility can be explored in human beings only in the form of adjuvant therapy for two reasons: 1. Moral and ethical considerations preclude the use of chemotherapy as the sole form of treatment when curative techniques are available. 2. Early tumors comparable to those utilized in animal experiments are diagnosed but rarely in man. Therefore, surgical excision of the gross tumor followed by chemotherapy for the residual cells appears to be the appropriate clinical experimental situation.

The Third Aim

The third aim of the cooperative group effort is to develop workable methods and techniques for therapeutic trials in cancer. Research in cancer has been retarded by lack of standard definitions of diagnosis, treatment, and response, with the result that series of clinical chemotherapeutic trials reported by different investigators are almost never directly comparable. Uniform criteria for admission of patients to the study, of the treatment schedule, and of subsequent observations are essential to a meaningful pooling or comparison of data. Pooling from several medical centers is desirable in order that an adequate number of patients for analysis can be gathered within a reasonable period of time.

As stated previously, these clinical studies are predicated upon the hypothesis that chemical materials which have some effectiveness against advanced human neoplasms may have greater effect when directed against much smaller, earlier distant deposits of the tumors, microscopic amounts of residual tumors, and unestablished tumor cells. It is evident, therefore, that the only reliable end-point of the investigations is the determination of survival in a sufficient number of patients treated with a chemical agent, as compared with the survival in an entirely comparable group of patients treated in an identical fashion but not receiving the adjuvant material.

Such comparability is possible only by the use of strict randomization procedures, through which patients enter the study group and the control group by laws of chance rather than by selection. A great advantage of this method is that a minimal number of patients is exposed to potentially dangerous procedures or agents in providing a reliable evaluation in the shortest possible time.

It is hoped that these studies will stimulate the initiation of similar strictly controlled group studies on the effectiveness of other types of treatment for cancer. For example, the addition of thousands of cases to the individual series already available on radical mastectomy and on simple mastectomy plus radiation would not clarify the essential issues. What is needed is a therapeutic trial in which such a comparison would be carried out with the patients entering each group on a randomized basis.

The Cooperative Studies

The present cooperative studies on the adjuvant use of chemotherapy in the surgical treatment of cancer were organized in November, 1956, under the leadership of the Clinical Studies Panel of the Cancer Chemotherapy National Service Center. The studies could not have been developed without the interest and support of Dr. I. S. Ravdin, chairman of the Clinical Studies Panel, and of Dr. K. M. Endicott, chief of the Chemotherapy Center.

The panel decided that the first studies should include neoplasms with a poor prognosis which were known to be affected by the chemotherapeutic agent employed and others which were considered insensitive to such chemicals. This decision led to the selection of two investigations, one on pulmonary carcinoma, with nitrogen mustard as the chemical adjuvant, and the other on gastric carcinoma, with Thio-TEPA for adjuvant chemotherapy.

The study plan, or protocol, for gastric carcinoma is representative of the experimental design of such studies. It was developed by a group of clinical investigators with the participation of statisticians. Since Thio-TEPA, the chemical proposed for trial, is a powerful hematopoietic depressant, a preliminary study was carried out by a number of participating clinicians to ascertain that the recommended dose schedule did not produce serious additional morbidity in surgically treated patients.

The following principles were agreed upon: (1) pooling of data from all institutions in order to accumulate rapidly the necessary number of patients; (2) standard criteria of diagnosis, treatment, and measurement of effect; (3) statistical design of the study, with randomized assignment of patients to the groups to be compared; and (4) statistical analysis and collaborative reporting of the results.

The protocol includes detailed definitions and instructions for the determination of patient eligibility, such as exclusion of patients with gastric lymphosarcoma and with metastatic lesions. It indicates the minimal clinical and laboratory procedures that must be performed preoperatively and postoperatively.

The exact surgical procedure of gastrectomy is left to the discretion of the surgeon, but unusual techniques are excluded. The patients are classified into three therapeutic categories: (1) total gastrectomy with curative intent, (2) partial gastrectomy with curative intent, and (3) total or partial gastrectomy with palliative intent. Patients with nonresectable lesions are excluded from the formal study.

Randomization of patients into the group receiving adjuvant chemotherapy and those not receiving chemotherapy is achieved by a closed envelope technique. The surgeon is not informed of the assignment of the patient until after the excisional procedure has been completed so as not to introduce any possible influence upon the kind or extent of the operation. It is only before the closing of the abdomen that an envelope prepared by the central statistical unit is opened and the assignment instructions therein are followed.

The schedule of administering Thio-TEPA to the patients falling into the chemotherapy group is as follows: Upon completion of the operation, 0.2 mg. per kilogram of body weight is injected into a portal vein and 0.2 mg. per kilogram into the peritoneal cavity. On the first and second postoperative days, 0.2 mg. per kilogram is injected intravenously, for a total dose of 0.8 mg. per kilogram of body weight during a period of three days. All Thio-TEPA is from one lot, prepared for intravenous use.

Follow-up examinations are designed to obtain information on the effect of the chemotherapeutic agent upon the hematopoietic system and on the subsequent course of the patient. Survival rather than recurrence or metastasis is adopted as the criterion of effect.

The flow-sheet of the study of gastric carcinoma is given in the figure.

All patients entering the study are reported to a central statistical unit as soon as the randomized assignment is made at the operating table. The closed envelope for this purpose contains a card for the report, and standard forms are provided for reporting the details of the status of the patient, of the operation, and of the follow-up. The importance of the central statistical unit cannot be overemphasized, since it has the responsibility of providing randomization instructions, indexing all patients admitted to the study, performing checks on the accuracy of the data, verifying survival periods, and, finally, assessing the effectiveness or lack of effectiveness of the experimental therapy. The results are being followed by a sequential method that allows early information and termination of the study if a statistically valid difference is observed. The pathology specimens are also centrally reviewed, at the Armed Forces Institute of Pathology.

It was estimated, on the basis of anticipated survival, that approximately 250 patients in the group receiving chemotherapy and 250 patients in the group not receiving chemotherapy should enter the investigation in order to reach the desired statistical determination of effect. In order to attain this number of patients within 18 to 24 months, 19 university departments of surgery and 20 Veterans Administration hospital departments of surgery are participating in the study. These groups are under the chairmanships of Dr. William P. Longmire of the School of Medicine of the University of California at Los Angeles and of Dr. John P. North of the Veterans' Administration Hospital in Dallas, Texas, respectively. The same protocol is used by both groups, and the results are statistically combined for analysis.

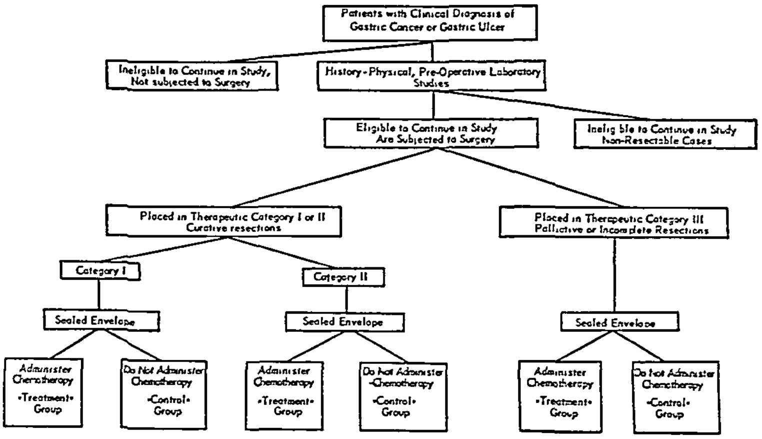
The participating surgeons meet at intervals to discuss their experiences and to clarify or modify the study plan as the group finds necessary. In all matters the safety and comfort of the patients is the paramount consideration. The poor prognosis of patients with gastric cancer should permit final assessment of the effectiveness of Thio-TEPA as an adjuvant chemotherapeutic agent against this tumor within two years after the necessary number of patients are entered in the study.

A second adjuvant chemotherapy study involves the use of nitrogen mustard in patients with resectable cancer of the lung. The study is quite similar to the one described for cancer of the stomach. The participants include 10 of the university surgical departments which are engaged in the gastric study, plus 8 other investigative groups and 21 Veterans Administration hospitals. The university group is under the chairmanship of Dr. Anthony R. Curreri of the Wisconsin University School of Medicine, and Dr. John P. North also serves as chairman of the VA hospitals' group on lung cancer.

Under consideration are additional studies on other sites of cancer, as well as the use of radioisotopes. The limited number of chemotherapeutic agents that demonstrate an effect on human cancer has restricted the present plans to the alkylating chemicals. It is obvious that any newer agents should first undergo wide trial in patients with cancer untreatable by customary techniques before they can be considered for use as adjuvants.

Summary

Under the auspices of the Cancer Chemotherapy National Service Center of the National Cancer Institute, 27 university surgery departments and 21 surgery departments of Veterans Administration hospitals have developed a statistically controlled *cooperative clinical study on the adjuvant use of* chemotherapy in the surgical treatment of cancer. Two investigations are now under way, the first using Thio-TEPA (triethylenethiophosphoramide) in resectable carcinoma of the stomach and the second using nitrogen mustard in resectable carcinoma of the lung. Statistically controlled cooperative studies will expose a minimal number of patients to the effects of a toxic agent in a minimal length of time and provide accurate appraisal of its effect.


Patients with Clinical Diagnosis of Gastric Cancer or Gastric Ulcer
Ineligible to Continue in Study, Not subjected to Surgery
History-Physical, Pre-Operative Laboratory Studies
Eligible to Continue in Study Are Subjected to Surgery
Ineligible to Continue in Study Non-Resectable Cases
Placed in Therapeutic Category I or II Curative resections
Placed in Therapeutic Category III Palliative or Incomplete Resections
Category I
Category II
Sealed Envelope
Sealed Envelope
Sealed Envelope
Administer Chemotherapy •Treatment• Group
Do Not Administer Chemotherapy •Control• Group
Administer Chemotherapy •Treatment• Group
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Do Not Administer Chemotherapy •Control• Group

Conduct of study of stomach tumors in adjuvant chemotherapy program.

The use of chemotherapy as an adjuvant to surgical treatment of cancer has the theoretical advantage of testing the effect of an agent on small amounts of residual tumor and on unestablished tumor cells. A review of pertinent experimental work suggests that an agent that is moderately effective against an advanced tumor may be curative against smaller tumors and unestablished cancer cells.

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"DRY" BRONCHIECTASIS

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Bronchiectasis is generally accompanied by a chronic cough with purulent sputum and occasional hemoptysis; when neither sputum nor blood is produced, the bronchiectasis is called dry. Among the 22 cases of dry bronchiectasis here analyzed, there were 7 in which pulmonary symptoms were absent; the patients in the latter group requested medical examination for such nonpulmonary symptoms as failing vision, dizziness, or chronic fatigue. Three cases are given to illustrate the occurrence of hemoptysis, the episodes of dry coughing, and the occasional absence of respiratory symptoms. The diagnosis was established by roentgenograms, which were made in all cases. Surgical treatment was resorted to in but two of these patients, one because the amount of bronchial secretion was excessive and the other because there had been two episodes of hemoptysis.

Not all patients with bronchiectasis exhibit the classic symptoms of chronic productive cough, hemoptysis, and recurrent acute respiratory infections. A minority have minimal or atypical symptoms; a few are asymptomatic, the disease being discovered during investigation for some other complaint.

The present review, prompted by our recent experience with several such patients, is an attempt to assess the frequency of occurrence and the principal clinical manifestations of so-called dry bronchiectasis and to uncover possible distinctive anatomic features that might explain the absence of classic bronchorrhea.

The present study includes 22 cases of dry bronchiectasis encountered at the Mayo Clinic in the three-year period from 1954 through 1956. This total represents about 3% of the entire number of patients found to have bronchiectasis during this period. The clinical records of all patients who

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underwent bronchography during those years were reviewed, and those cases in which symptoms were atypical were selected for study. Posteroanterior stereoscopic roentgenograms of the thorax had been made in all of these patients during their medical examination. A bronchoscopic examination was performed in each instance in conjunction with, or on the day previous to, bronchography, so that the appearance of the bronchial mucosa and the presence or absence of secretion were noted.

Clinical Features

Ten patients were in the fifth decade of life, eight in the sixth, two in the third, and one each in the second and fourth decades. There were 8 males and 14 females.

Pulmonary History.—Eight patients had no history of previous pulmonary disease of any kind. Nine patients had had pneumonia, three during childhood and the remainder at some time during the preceding 10 years. Two patients gave histories of old and clinically inactive tuberculosis. One patient had had hemothorax of undetermined cause 2 years before, and one had experienced spontaneous pneumothorax 20 years previously. The remaining patient recalled having had pertussis in childhood.

Signs and Symptoms.—The clinical features were such that the patients could be classified into three groups. The first group included 13 patients who complained of previous hemoptysis, varying from one brief episode to recurrent bouts for several years; 3 of these patients also had chronic or occasional unproductive cough. The second group consisted of two patients who had only occasional unproductive cough. The third group comprised seven patients who did not have any pulmonary symptoms; they had requested medical examination for such nonpulmonary symptoms as failing vision, dizziness, or chronic fatigue. In the second and third groups of patients, abnormalities seen on routine roentgenograms of the thorax led to bronchoscopic and bronchographic studies that delineated the underlying abnormality. Routine roentgenography of the thorax showed abnormalities in only 6 of the 13 patients in group one. The history of hemoptysis prompted the endoscopic procedures in this group.

Physical findings were significant in eight patients, depression of breath sounds on one side being noted in five and transient rales in three. Examination of the thorax revealed no abnormalities in the remaining 14 patients.

Roentgenography.—Posteroanterior stereoscopic roentgenograms were interpreted as normal in 7 patients, with positive findings being noted in the remaining 15. The alterations varied from minimal increase in bronchovascular markings to changes that were sufficiently marked to suggest to the roentgenologist the likelihood of bronchiectasis.

As already indicated, bronchograms were made in all cases. The extent and distribution of the disease process varied considerably. The location of the bronchiectasis was as follows: Right lung—upper, 6; middle, 10; lower, 10. Left lung—upper 3; lingula, 6; lower, 9. Two or more lobes frequently were involved. Thus, the most commonly affected regions were the right middle and lower lobes, followed closely by the left lower lobe. It is generally accepted that bronchiectasis in the upper lobes has a tendency to produce fewer symptoms because of the natural bronchial drainage enjoyed by these regions. Thus, it is interesting to note that the upper lobes were not predominantly affected in this series.

In all cases in which the posteroanterior stereoscopic roentgenogram of the thorax revealed an abnormality, the bronchograms revealed bronchiectasis in the same zone. The disease was confined to this location in seven cases, while it was present also in other regions, sometimes on the opposite side, in eight others. In no case did bronchography fail to show disease in a zone designated as abnormal on the routine thoracic roentgenogram.

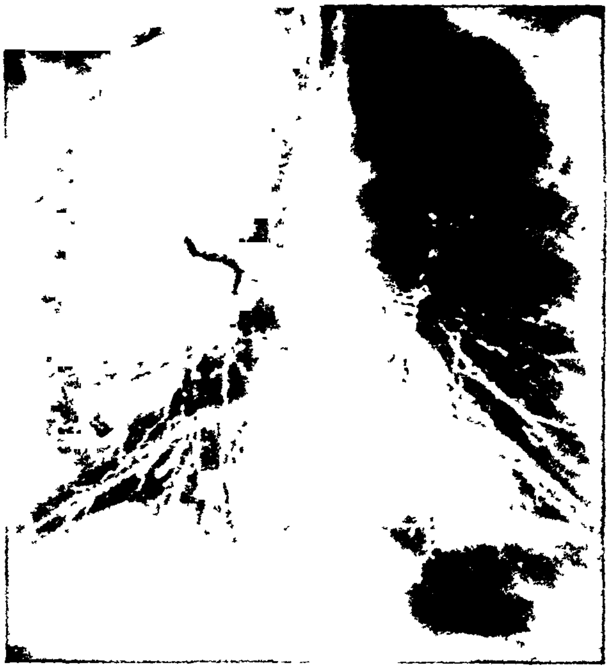

Fig. 1 (case 1).—Posteroanterior bronchogram revealing scattered saccular bronchiectasis involving bronchi in posterior basal segment of right lower lobe. The only respiratory symptom was occasional brief hemoptysis. The routine posteroanterior roentgenogram of the thorax was normal.

Bronchoscopy.—Bronchoscopic examination revealed no abnormalities in eight patients. In the remaining 14 cases, blood was detected five times, some distortion of the bronchial tree was noted on three occasions, and bronchitis was found in six patients. Five of these last six patients had an abnormal increase in volume of bronchial secretions; usually, however, this increase was slight.

Treatment

Resection of involved bronchopulmonary segments was done in only two cases, the symptoms in the others being so minor that the physician or the patient did not consider that a major operation was warranted. Hemoptysis occurring on two previous occasions was the indication for resection in one patient. Resection also was performed on an 18-year-old girl, the youngest patient in this series. She had had frequent winter colds and was found to have sinusitis and nasal polyposis also requiring surgical treatment. Bronchoscopy revealed the largest amount of bronchial secretions of any patient in this study. Although her only pulmonary complaint was "dry" cough, she obviously had been swallowing the excess secretions.

Report of Cases

The following three brief case reports represent the three types of presenting clinical problems encountered in this series, namely, hemoptysis (case 1), occasional dry cough (case 2), and absence of respiratory symptoms (case 3). Also of interest is the fact that examples of cylindric and saccular bronchiectasis are included.

Case 1.—A 27-year-old housewife was referred to the Mayo Clinic in November, 1954, because of three previous bouts of scanty hemoptysis occurring in January and March, 1952, and in March, 1954. She denied having sputum except during colds. Physical examination revealed obesity but no other abnormalities. Bronchoscopy disclosed a small amount of inflammatory reaction in the bronchi of both lower lobes; however, not enough secretion was present to obtain a specimen for culture without preliminary bronchial irrigation with an isotonic solution of sodium chloride. Bronchograms using 20 ml. of iodized and chlorinated peanut oil (Iodochlorol) revealed saccular bronchiectasis involving the lateral and posterior basal divisions of the right lower lobe (fig. 1).

Case 2.—A 43-year-old scout executive registered at the clinic because of lifelong difficulty with drainage from the left ear. This had been treated surgically four years previously by the surgical construction of a nasoantral window and by tonsillectomy and adenoidectomy. Mastoidectomy had been performed in 1946. Although he had experienced three attacks of pneumonia in the previous six years, he denied any cough except on rare occasions.

Physical examination revealed a moist cavity resulting from the left radical mastoidectomy. Profound deafness was present on the left, but signs of active local infection were absent. Breath sounds were diminished posteriorly over the base of the left lung. A posteroanterior thoracic roentgenogram showed the mediastinal structures to be displaced to the left (fig. 2a).

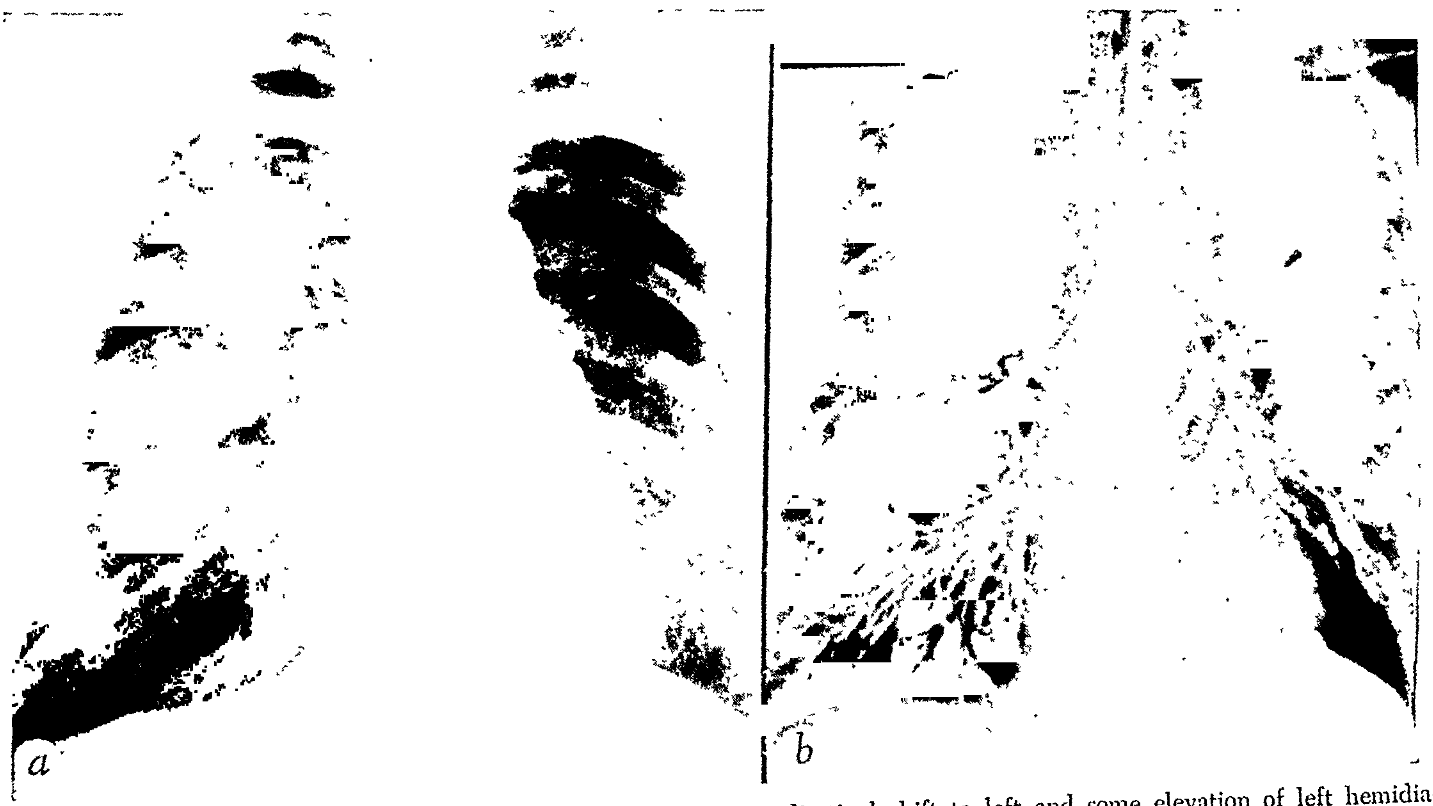

Fig. 2 (case 2).—*a*, posteroanterior roentgenogram showing mediastinal shift to left and some elevation of left hemidiaphragm. Scattered calcification is present, more prominent in the right lung field. *b*, posteroanterior view of bilateral bronchogram showing stenosis and angulation of left main bronchus with extensive bronchiectasis involving all major segments of left lung.

Bronchoscopy revealed slight narrowing and displacement of the left main-stem bronchus toward the midline. The bronchial secretions were not excessive. A dose of 20 ml. of propyliodone (propyl ester of 3, 5 diiodo-4-pyridone-*N*-acetic acid in water suspension with carboxymethylcellulose added [Dionosil]) in oil was instilled into each main bronchus; bronchograms revealed constriction of the left main bronchus, with bronchiectasis involving all of the segmental bronchi in the left lung (fig. 2*b*). The bronchi of the right lung were entirely normal. Cultures of bronchial washings were negative for acid-fast bacilli and fungi. Special studies did not reveal any malignant cells in the secretions.

Case 3.—A 42-year-old woman requested examination while she was accompanying her husband, who was a patient, through the clinic. She complained of a constant tired feeling, worse in the morning on arising. Physical examination revealed a small nodular goiter but no other abnormalities. Routine stereoscopic roentgenograms of the thorax disclosed a shadow at the right cardiophrenic angle (fig. 3*a*). Because of the indeterminate nature of this asymptomatic intrathoracic lesion, bronchoscopy was carried out but it showed only normal tracheobronchial mucosa. A total of 28 ml of propyliodone in oil was instilled into the right mainstem bronchus, and the resulting bronchogram revealed extensive saccular and cylindric bronchiectasis involving all divisions of the right upper and lower lobes (fig. 3*b*).

Comment

Bronchiectasis of varying distribution and severity can occur without causing the usual symptoms of cough with voluminous sputum or repeated bronchopulmonary infections. The criteria for making a diagnosis of "dry" bronchiectasis, as observed in the medical literature, are somewhat varied. The more liberal requirements include absence of a significant amount of sputum, whereas more rigid standards of finding bronchoscopically normal bronchial mucosa and absence of increased secretions also have been advocated.

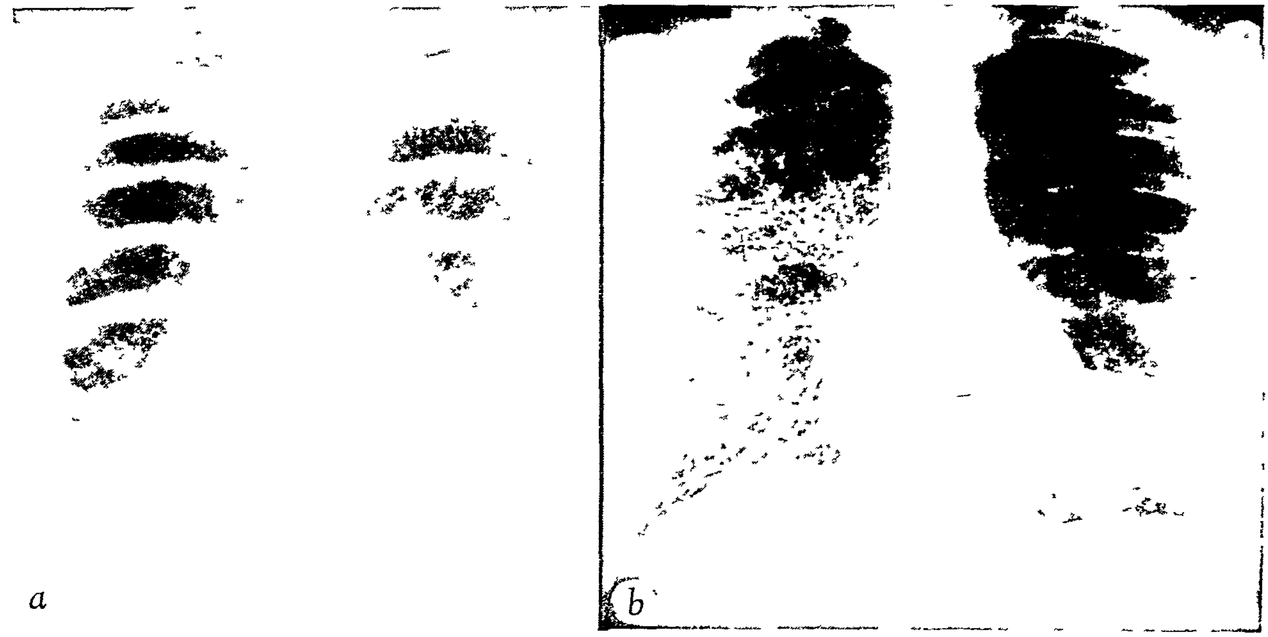

Fig 3 (case 3).—*a*, routine roentgenogram showing asymptomatic density at right cardiophrenic angle. Slight fibrosis also is present in the right midlung field *b*, right bronchogram revealing widespread bronchiectasis involving much of upper and middle lobes, as well as medial basal and superior segments of right lower lobe.

The term apparently was used first by Bezançon and associates[1] in 1924, in describing two cases in which the only symptom was recurrent episodes of hemoptysis. In a review of 23 cases of bronchiectasis in children published in 1927, Findlay and Graham[2] stated that the disease may be present when there is no clinical evidence of its existence. However, a history of cough was elicited in all but one of their patients, and a history of the production of sputum was present in 19.

Pinchin and Morlock[3] described a series of cases of dry bronchiectasis in 1930. A clear history of antecedent infection was present in the majority of these. In the same year, Burrell and Trail[4] reported the case of a 23-year-old man in whom the first and only symptom of bronchiectasis was copious hemoptysis.

In 1933, Wall and Hoyle[5] reviewed all cases of dry bronchiestasis reported up to that time, a total of 30, and added 20 cases of their own. However, sputum was definitely absent in only 9 of their 20 cases, so their designation of "dry" is perhaps too liberal. These authors noted that the diagnosis of bronchiectasis in many of the previously reported cases was made in the course of an investigation of patients having bouts of unexplained hemoptysis.

In a review of 106 cases of bronchiectasis, Roles and Todd[6] used a classification that included "dry" types, but it is not clear just how many of their patients did not produce sputum. Bronchoscopic examinations, if performed, were not mentioned.

Warner[7] stated that the infection in a bronchiectatic zone may diminish gradually so that ultimately there is no bronchorrhea and a stage of dry bronchiectasis is the result. He noted that such cases were unusual and that they comprised only about 2% of his series.

In a study of 100 patients with bronchiectasis, Farrell[8] noted that 99% had a cough and 91% had sputum. He made no reference to dry bronchiectasis. Ogilvie[9] stated that persistent cough was an original symptom in all of his 68 cases; it was not productive in 8 cases. Although dry phases occurred in many of his patients, he concluded that he was unable to establish with certainty the existence of dry bronchiectasis. He emphasized further that the bronchial mucosa should be dry and uninfected, as demonstrated by bronchoscopy, before the adjective "dry" could be used correctly to categorize such cases; he was unable to demonstrate this in the eight cases in his series in which the cough was not productive, although bronchoscopic examination was not performed in four of them.

In 1942, Martin and Berridge[10] reported 25 cases of bronchiectasis in soldiers who were graded A-1 in the Army. Cough and sputum were the presenting complaints in 23, dry pleurisy in one, and evening fever in one. Only the patient with pleurisy was incapacitated.

Fine and Steinhausen[11] reviewed 41 cases of bronchiectasis discovered through the use of routine thoracic roentgenograms in service personnel. None of these persons were incapacitated, and 20 originally denied all symptoms. Follow-up studies were made in 36 of the 41, some for as long as two years. Of those, 8 had no symptoms and 20 had minimal symptoms. When the disease was originally detected, all of the men were performing full military duty.

In a discussion of bronchiectasis published in 1951, Overholt[12] stated that symptomatic bronchiectasis may be converted to a dry type if infection is overcome. In a classification of categories of bronchiectasis, he listed "dry types of minimal symptoms" and noted that the first evidence in these patients was usually hemoptysis.

In a report on 166 patients with proved bronchiectasis in 1953, Wynn-Williams[13] stated that cough was absent in 12 and sputum was absent in 24, of whom 12 were children. The author stated that the cough was less severe and the sputum smaller in quantity in his patients than in those in many other reported series. It is generally appreciated that children swallow bronchial secretions more frequently than do adults, who more often expectorate the material from the hypopharynx.

In 1955, Lindskog and Hubbell[14] reported a study of 215 cases of bronchiectasis. Patients with dry or asymptomatic bronchiectasis were not described as such, although minimal symptoms were noted as having occurred in eight patients.

Thus, it is apparent that many reports have included examples of dry bronchiectasis, although the incidence is always low. Not all authors used the term as originally employed by Bezançon and associates.

The practical implication of this and similar reports is that bronchiectasis may occur in patients who have no symptoms or who present symptoms unrelated to increased or retained bronchial secretions. A patient who has bronchiectasis and who coughs but does not expectorate may be swallowing sputum. However, most of the patients in our series did not have even a dry cough, or at least they denied it. Bronchoscopy revealed absence of bronchial inflammation or hypersecretion in 16 of the 22 patients. This would support the clinical feature of absence of cough in the majority of these patients. Five of the patients who were found to have excess secretion at bronchoscopy most likely were swallowing the secretions. Since the bronchial mucosa was normal and free of excess secretions in the majority of patients, some additional factor must account for the clinical absence of expectoration.

The reason for absence of an excess of bronchial secretions in this group of patients with bronchiectasis is not known. Furthermore, the exact mechanism of elimination of the normal and abnormal bronchial secretions is not precisely known. Ogilvie, in his extensive review, commented on numerous studies of the ciliary action and possible peristalsis of the muscularis in elimination of bronchial secretions. As early as 1929, Macklin[15] reviewed extensively the physiological studies on the musculature of the bronchi and lungs. More recently, the patterns of flow of mucus[16] and the rate of the ciliary beat[17] have been described as a result of newer techniques of investigation. As more is learned about these basic functions, an explanation of these atypical cases of bronchiectasis may be forthcoming. One can only speculate at present that the mechanism of elimination of secretions is either recovery in the bronchiectatic regions or, in the absence of such recovery, the ability of the bronchial branches distal to the affected zone somehow to decrease or resorb[18] the secretions.

Summary

The clinical features in 22 cases of "dry" bronchiectasis encountered at the Mayo Clinic were reviewed. Hemoptysis, usually considered the prime warning sign leading to discovery of such cases, was observed in only slightly more than half of the cases. The discovery of an abnormal pulmonary shadow in the thoracic roentgenogram in patients without respiratory symptoms was a common finding in this study. The combination of occasional nonproductive cough and an abnormal pulmonary roentgenographic shadow was the least frequent in this series.

The clinical picture of dry bronchiectasis was not related to the lobar or segmental distribution, the number of segments involved, the type of deformity of the segments involved, the age of the patient, or the history of previous tuberculosis. This syndrome accounted for only about 3% of all cases of bronchiectasis diagnosed during a recent three-year period.

Surgical resection of the involved pulmonary segments was advised only in two cases. Minimal or absent symptoms in most cases warranted only continued observation once the diagnosis was established.

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TREATMENT OF EIGHT CASES OF HYPERTHYROIDISM WITH COBALTOUS CHLORIDE

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Eight patients with hyperthyroidism were treated with cobaltous chloride by mouth. Clinical improvement was manifested by abatement of the tachycardia, reduction of basal metabolic rate, and rise in red blood cell count and blood hemoglobin content in four patients These four patients also gave striking evidence of improvement in laboratory tests with radioiodine and three of them underwent thyroidectomy without complication after the cobalt therapy alone. The other four patients had less favorable results. One showed improvement in her preexisting anemia but suffered recurrence (after temporary relief) of her symptoms of hyperthyroidism despite continued cobalt therapy; the other three did not respond to the cobalt at all as regarded their hypothyroidism, although one showed marked hematological improvement. The mode of action and indications for the use of cobalt in hyperthyroidism require further study.

Kriss, Carnes, and Gross[1] reported in 1955 the development of thyroid hyperplasia in four children and one adult receiving cobaltous chloride by mouth in doses ranging from 2.8 to 3.9 mg per kilogram per day. In three subjects, in whom radioiodine (I ^{131}) studies were done, it was found that thyroid I ^{131} uptake was markedly depressed. Jaimet and Thode[2] have thrown serious doubts on those findings, since they were unable to demon-

TABLE 1.—*Chief Symptoms and Signs*

Case No	Age, Yr	Sex	Duration of Symptoms, Mo	Loss of weight, Kg	Nervousness	Exophthalmos	Goiter*
1	47	F	8	12	++	+	D1
2	24	F	12	30	++++	+	D3
3	24	M	24	15	++++	+	D3
4	50	F	48	++	++	+	D2
5	27	F	7	+++	++++	++	N3
6	22	M	3	30	++++	++	N2
7	35	F	1	++	+++	++	D3
8	13	F	7	++	++++	+	D2

* D=diffuse, N=nodular; 1=barely palpable, 2=palpable and visible; 3=grossly visible

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strate consistent effects of cobalt (in doses up to 6 mg. per kilogram per day) on thyroid I ^{131} uptake, conversion ratios, and saliva radioactivity. More recently, however, Roche and Layrisse[3] have shown that cobaltous chloride in doses of 150 mg. per day in 12 nonanemic euthyroid adults led to a distinct fall in thyroid I ^{131} uptake, in most cases after one week and in all cases after two weeks. In view of these findings, it was deemed worthwhile to try cobaltous chloride therapy as a means of controlling hyperthyroidism.

Table 2.—*Treatment and Clinical Course*

Case No.	Cobaltous Chloride, Mg./Day	No. of Days Given	Clinical Improvement	Apparent Increase in Goiter	Pulse/Min.* A	Pulse/Min.* B	Weight, Kg.* A	Weight, Kg.* B	Subtotal Thyroidectomy	Other Treatment
1	150 300	55 31	++++	0	130	80	53	53	+	Propylthiouracil; stopped 1½ mo. before cobalt started
2	300 0 150 300	3 1 8 34	++++	0	113	88	43	46	+	
3	300 300	30† 15	++++	0	100	80	61	61	+	
4	300 0 150	15 1 117	+++	0	100	80	41	41	...	
5	150 300	54 16	++	+++	130	94	39	46	+	Lugol's solution, 20 drops, t.i.d last 25 days
6	600 300	10 16	0	+	104	110	61	60	...	No response to methimazole or to perchlorate treatment; finally controlled with 16 mc. of I^{131}
7	300 150 300	6 3 30	0	++	130	104	50	50	+	Response to methimazole
8	300 150 300	1 3 40	0	0	130	114	37	37	+	Response to methimazole

* A=before treatment; B= at the end of treatment.

† This patient was ambulatory during the first 30 days of treatment and it was felt that he did not take his medicament properly during this time.

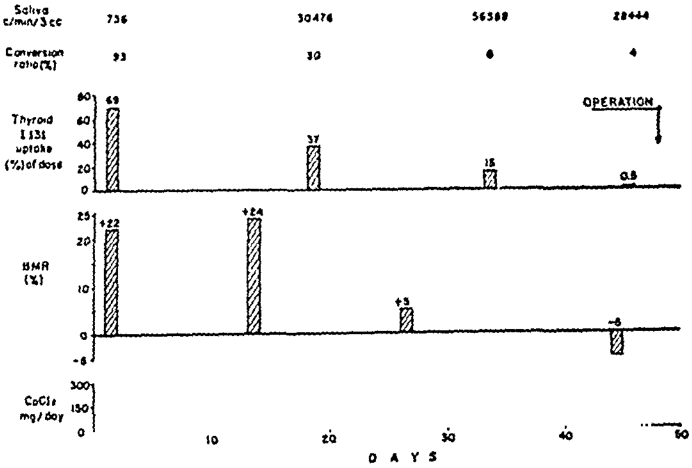

Fig. 1 (case 2).—Good response to cobalt therapy. Thyroidectomy.

Eight cases of hyperthyroidism treated with cobaltous chloride are herein reported. In four of the cases there was marked clinical improvement, and in three of these a thyroidectomy was performed without complication after cobalt therapy alone (cases 1 and 2 have been briefly reported[3]). In one case, there was initial response and later "escape," making it necessary to administer Lugol's solution before thyroidectomy; in the three remaining cases, there was no response to cobalt.

Methods and Material

Thyroid uptakes were determined with a scintillation counter (Nuclear, model DS-1), saliva radioactivity,[4] and conversion ratios[5] with a well-type scintillation counter (Nuclear, model 3037 B) 24 hours after the administration of 50 μc of I ^{131}, correction being made if necessary for residual radioactivity. Cobalt was administered by mouth as cobaltous chloride in a 1% solution, in three divided doses after meals. The pulse was taken in the morning upon awakening.

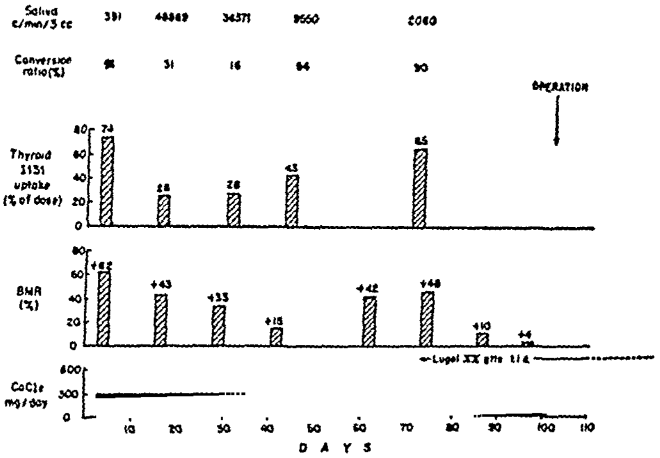

Fig. 2 (case 5).—Initial good response to cobalt therapy and later "escape." The administration of Lugol's solution in addition to cobalt led to rapid remission of the hyperthyroidism. Lugol's solution was continued after operation.

All patients were hospitalized in the Hospital Vargas. The chief symptoms and signs are given in table 1 and the treatment indicated in table 2. Histological study was performed on all thyroid glands removed at operation.

Results

The clinical course is summarized in table 2 and the chief laboratory findings before and at the end of treatment in table 3. Intolerance to medication in the form of epigastric pain, burning, and nausea was experienced by four patients, generally toward the start of treatment, while all other patients tolerated treatment well.

In one additional patient, treatment with cobalt could not be continued because of gastric intolerance to the drug. In the cases presented here, it was not necessary to discontinue medication entirely; in general, it was sufficient to stop cobalt for a day or two and resume therapy at a lower dosage level After a week or two, the dosage could be raised again to its initial level without further trouble.

Comment

In five of the eight patients with hyperthyroidism treated with cobaltous chloride, there was clear-cut remission of symptoms and laboratory evidence of blocking of thyroid hormone synthesis.

Although it is well recognized that hyperthyroidism may subside spontaneously, it is unlikely that this should occur in five cases out of eight during a relatively short period of observation. In the early reports collected by Sattler,[6] spontaneous remission is said to have occurred in from none to 50% of mild unoperated cases, with an average of 26%, recovery was described as usually occurring several years after onset. Since practically all patients today receive antithyroid treatment, there are no recent figures available on this point.[6] Furthermore, we do not believe that a spontaneous remission would explain the laboratory evidence of block of thyroid hormone synthesis.

It was possible to perform thyroidectomy on three of the five patients who responded to cobalt without the addition of any other antithyroid medication. In one of the patients, who objected to operation (case 4), it was possible to continue cobalt therapy for 117 days without any untoward effect. After medication was discontinued, there was no return of symptoms, the patient died two months later of a cerebrovascular accident.

TABLE 3 —*Effect of Cobaltous Chloride on Laboratory Tests*

	Blood Hemoglobin Level Gm /100 Ml *		Red Blood Cells Million Ml *		BMR, %*		24 Hr I131 Thyroid Uptake, %*		Conversion Ratio, %*		Saliva Radioactivity, 1,000 Counts/ Min /3Cc *	
Case No	A	B	A	B	A	B	A	B	A	B	A	B
Response												
1	13.3	15.0	4.2	4.7	−59	−1	75	17	76	[illegible]	5.3	53.9
2	11.5	15.0	3.9	4.4	−22	−5	69	0	93	4	0.7	56.4
3	13.8	17.7	4.4	5.1	−25	−6	51	17	92	6	0.2	61.2
4	10.4	14.0	3.5	4.3	−44	−1	76	1	83	7	0.3	125.7
Response and "escape"												
5†	11.7	15.0	3.9	4.5	−62	+46	74	65	91	90	0.4	2.0
No response												
6	13.1	14.3	4.5	4.5	+55	.	75	59	83	91	2.1	4.4
7	8.7	13.0	3.0	4.2	−31		55	49	93	86	1.6	8.5
8	9.1	9.1	3.3	3.0	+44	−21	58	42	93	87	0.8	5.6

* A=before treatment, B=after treatment with cobalt

† This patient "escaped" treatment The levels reached before escape were BMR, −15, thyroid uptake, 26, conversion ratio, 16, saliva radioactivity, 48.9

The data on one of the patients who responded to cobalt (case 2) are presented in figure 1. In this case, the initial dose was 300 mg. of cobaltous chloride per day. This had to be stopped after three days because of nausea and epigastric distress. After 24 hours off treatment, cobalt therapy was resumed, at a dose of 150 mg. per day, without difficulty, so that after a week the initial dosage could again be started. There was definite clinical improvement after three weeks, associated with evidence of block in thyroid hormone synthesis, and a decrease in basal metabolic rate (BMR) to normal levels. Thyroidectomy was performed 45 days after the beginning of cobalt therapy.

In one patient (case 5) (fig 2) there was clinical improvement at first and evidence of thyroid block. After 30 days of treatment, pulse and nervousness began again to increase and there was evidence of renewed thyroid activity. the goiter had increased markedly in size, and on the 70th day while cobalt therapy was being continued, Lugol's solution, 20 drops three times a day, was added, with resulting rapid and marked clinical improvement. Thyroidectomy was performed within 30 days of starting therapy with Lugol's solution. It is interesting that this patient had a nodular goiter, in which resistance to therapy is frequently observed.

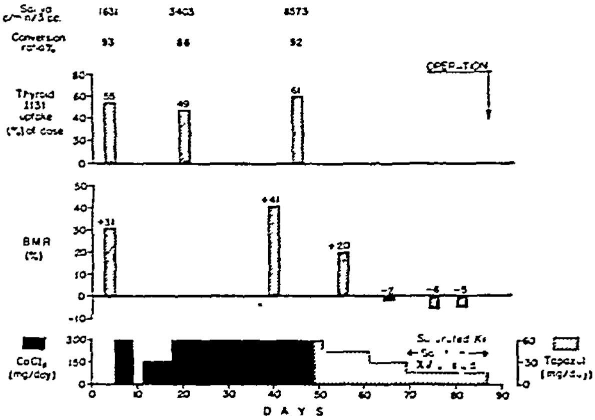

Fig. 3 (case 7).—No response to cobalt therapy. Good response to methimazole.

Finally, in three cases, there was no response to therapy, even though cobalt was given in doses similar to those given in the previous four cases. The data on one such patient (case 7) are shown in figure 3. In spite of the administration of cobalt for 45 days, there was no change in clinical status, thyroid uptake, conversion ratio, BMR, or saliva radioactivity. Treatment with methimazole (Tapazole) resulted in rapid improvement, and thyroidectomy was performed after the addition of saturated potassium iodide solution. One of the three patients who did not respond to cobalt (case 6) had also a nodular goiter, and there was no response to drug therapy with methimazole or with potassium perchlorate. Hyperthyroidism was finally controlled in this case with 16 mc. of I^{131}.

In all of the patients who responded to cobalt, blood hemoglobin levels and red blood cell counts rose under therapy (table 3). Of the three patients whose thyroid status did not change with cobalt, only one (case 7) showed a distinct rise in hemoglobin and red blood cell count, but this could not be attributed to cobalt, since this patient was given ferrous sulfate therapy simultaneously. The lack of response in the hematological indexes of two patients (cases 6 and 8) would suggest that, in these cases at least, cobalt was not properly absorbed and therefore did not reach in sufficient concentration either the thyroid gland or the bone marrow.

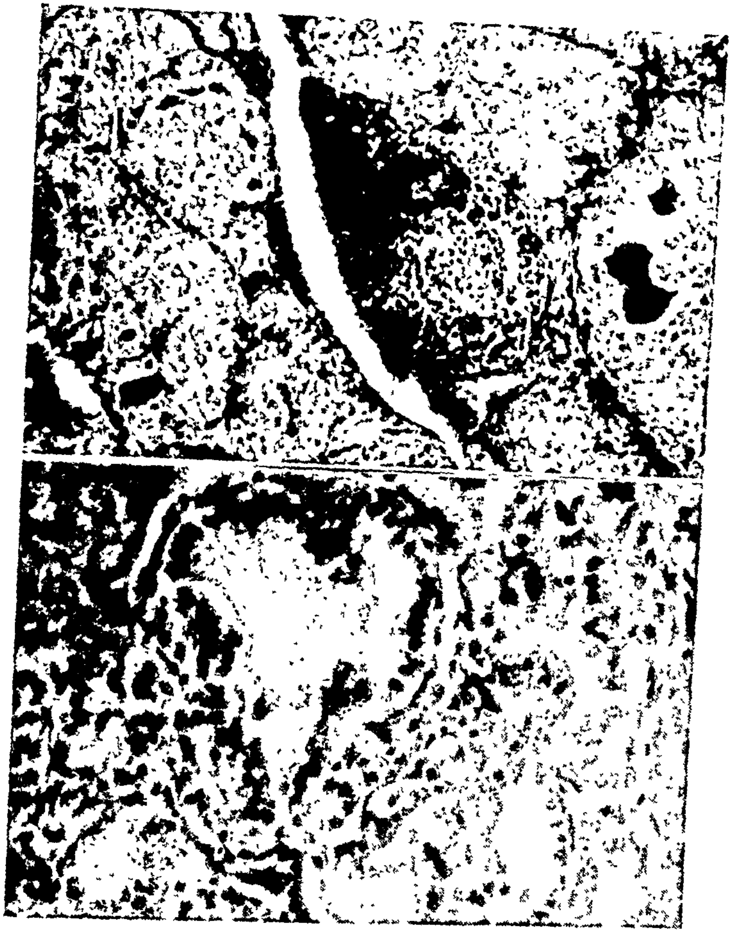

Fig. 4.—*Top,* thyroid tissue from patient in case 2. Thyroid hyperplasia, high epithelium, sparse colloid; in the center, accumulation of lymphocytes (hematoxylin-eosin stain, × 150). *Bottom,* thyroid tissue from patient in case 1; infolding epithelium; sparse colloid with abundant vacuoles (hematoxylin-eosin stain, × 300).

Histological study of the thyroid glands removed at operation (fig. 4) after cobalt treatment alone showed marked hyperplasia of follicular tissue with a high columnar, infolded epithelium. The sparse colloid contained abundant vacuoles. This appearance is not unlike that seen in patients treated with antithyroid drugs of the thiouracil type.

Cobalt appears to be clearly capable of blocking thyroid hormone synthesis in hyperfunctioning thyroid glands, as it does in normal thyroid,[3] although its action is somewhat unpredictable, as witnessed by the three patients who showed no response whatever. The reason for this lack of response is at present unclear, as is in fact the mechanism of cobalt action on the thyroid. We feel, however, that, in view of the good results obtained in several of the cases, it might be interesting to submit this drug to further therapeutic trial in hyperthyroidism.

Summary

Eight patients with hyperthyroidism were treated with varying doses of cobaltous chloride by mouth. In four of these, there was marked clinical improvement and evidence of block of thyroid hormone synthesis. In three of these cases a thyroidectomy was performed; the histological appearance was that of follicular hyperplasia. One of the four patients who responded was carried for 117 days on cobalt therapy, with apparent clinical remission. One patient who responded initially later "escaped" the effect of the drug and had to be given Lugol's solution before operation. In three cases, there was no response to the drug; one of these patients did not respond to methimazole or potassium perchlorate, and had to be given I^{131} therapy.

Apartado 1827 (Dr. Roche).

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MOBILE EEG DIAGNOSTIC UNIT OF THE MICHIGAN EPILEPSY CENTER AND ASSOCIATION

Adele L. Rolfe, M.S.W., Arthur J. Derbyshire, Ph.D.
and
Z. Stephen Bohn, M.D., Detroit

The total mobile unit service of the Michigan Epilepsy Center and Association (MECA) includes electroencephalography (EEG), neurological consultation, neurological examination, and lectures on epilepsy. From the physician's referral information and the patient's previous medical and hospital contacts and social-medical history, the neurologist adds to the EEG report his diagnostic considerations and suggestions for the continued management of the patient. The referring physician therefore receives both the EEG report and neurological consultation. The very presence of this diagnostic laboratory in an area tends to strengthen the patient-doctor relationship in many instances. One major problem for the mobile unit, which is still not satisfactorily solved, concerns the ideal for which the MECA stands, namely, a total approach, with use of many medical and allied disciplines to determine the causes and the treatment program for each patient.

In 1947, the Michigan Epilepsy Center and Association (MECA) came into existence with a grant from the Society for Crippled Children and Disabled Adults, through its state organization, Detroit and Dearborn Chapters. Three years later the Michigan United Fund assumed the support of the center. This change brought with it increased responsibility to the residents of the state of Michigan for service in the area of epilepsy. Dr. R. Dixon, who was our medical director at that time, and who had recently retired as medical superintendent of Caro State Hospital for Epileptics, suggested a traveling electroencephalography (EEG) service. At that time only two of the four EEG centers in the state were open to use by general practitioners, and these were below the center of the state. There were, however, rumors of the establishment of two additional EEG facilities. In fact, in accordance with the distribution of the population of the state, about 50% lived outside of counties with EEG laboratories. Dr. Dixon's suggestion was to put an EEG unit into a suitable truck and tour the areas of Michigan where EEG service was not readily available. In the summer of 1951 under the direction of Mrs. T. E. Kidder, a traveling EEG unit was put on the road for the first time.

One major problem of our program for the mobile unit, which is still not satisfactorily solved, concerns the ideal for which the MECA stands, namely, a total approach, using many medical and allied disciplines to determine the causes and the treatment program for each patient. A mobile EEG service tends to deny this and perhaps places the EEG in the dubious position of being called upon to form the sole basis for diagnosis. What it can accomplish, however, far outweighs these deterring aspects. This program can (1) offer the medical practitioner the information gained by EEG for the benefit of the patient (the test will confirm his impressions, help in evaluating severity of disturbance, and find possible foci for seizures, as well as contribute to treatment plan); (2) increase the awareness of the physician in treatment possibilities; (3) increase the understanding of the general population about epileptic people and their illness; and (4) encourage, through its use, interest in developing additional local EEG facilities as permanent installations.

Around any such permanent installations stimulated by the mobile program the center can develop the total approach, as it has been developed in Detroit. Here, each referred patient is seen by a neurologist, an internist, a psychiatrist, a pediatrician, a neurophysiologist, a social worker, a psychologist, and a religious consultant. Through mutual discussion, their information about the patient is synthesized into a diagnosis with probable etiologies and appropriate treatment recommendations covering all areas studied.

While falling far short of such a total study, the mobile unit has added, as money has become available, neurological consultation. It has always been the hope to broaden the approach through permanent facilities, or, as a second choice, to expand the mobile services.

Method

Description of Mobile Laboratory.—Finances limited the traveling program to a 10-week period, and weather conditions throughout northern Michigan, which was our primary target, limited the program to the summer. Finances further limited us to producing an EEG technician who was also a truck

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Administrative Director of State-Wide Mobile Program (Miss Rolfe); Chairman of the Research Planning Team and Consulting Neurophysiologist (Dr. Derbyshire); and Medical Director (Dr. Bohn), Michigan Epilepsy Center and Association.

driver with a chauffeur's license. Finances again limited us to a moving vehicle of such size that it could be sleeping quarters, office, and EEG laboratory, all in one. A friend of the center, hearing of our needs, offered us the loan of a new 2½-ton trailer of the type used for moving furniture; we would have to rent the tractor. In this large van were such items as a cot, a large easy chair for the patient during the EEG test, an eight-channel Grass EEG instrument, a table, and chairs.

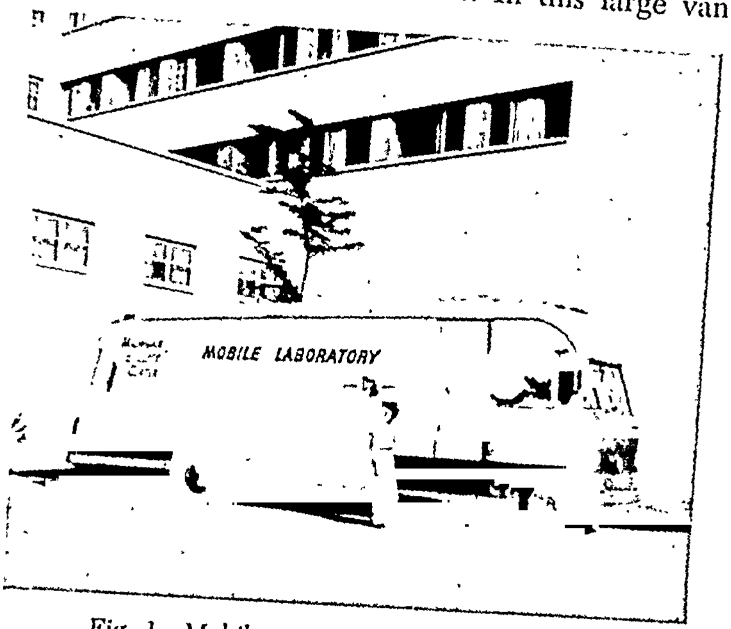

Fig. 1.—Mobile unit parked behind hospital.

The following year this mobile equipment was replaced by a house trailer and a pickup truck, and in 1954 we were given the present equipment (fig. 1 and 2), which consists of a paneled single-unit truck, donated by a large electrical manufacturing firm. This truck, 30 ft. long by 8 ft. wide by 11 ft. high, was originally custom-built in Ohio for the purpose of displaying electrical equipment. We easily adapted it to our use by dividing the space with a curtain into living and working quarters for two people. It can be driven into any small hospital or clinic grounds, where the unit can obtain water through a 100-ft. hose and its needed 2,000 watts of 110 AC power through a 100-ft. electric extension cable. As assurance against power failure, there is a gasoline-driven generator in the rear of the truck, which can supply enough power with adequate frequency (60-cycle) control to obtain reliable recordings. Derryberry[1] describes a similar truck used for mobile chest x-rays.

The Grass Instrument Company supplied us with a special rubber mounting, such as is used for fastening an engine block to a chassis. Through this, the EEG instrument is bolted to the floor during transportation. It can be unbolted and wheeled about the truck once the unit is parked. The problem of electrical grounding is solved by connecting the ground post of the EEG instrument to the metal structure of the truck. This uses the grounded side of the AC supply as the one common grounding point for both the EEG instrument and the metal body of the truck. The metal body, therefore, becomes the electric shielding. The only troubles which develop occur when the unit is parked under a transformer or when in a heavy rain a double ground is made by the water rising to contact some metal part or wheel of the truck. In most situations less artifact of 60-cycle pickup is encountered than in many hospital laboratories.

In selecting personnel to operate the mobile unit, it has been our experience that the most interested and resourceful technician can be developed in medical or premedical students. The job offers them opportunity to learn more about neurophysiology, history taking, and patient contact and invaluable experience in working with established medical practitioners throughout the state where the medical student is eventually most likely to practice.

We receive in return, from the medical student, a dedicated kind of interest in patients. They have an enthusiastic and warm center-doctor relationship, an insatiable curiosity to develop their understanding in the area of epilepsy, and a medical orientation and vocabulary for this work.

Services Offered.—The total mobile unit service includes EEG, neurological consultation, neurological examination, and lectures on epilepsy. The EEG service offers a standard half-hour test, which can reveal a localization as well as description of general pattern. In addition, activation is often tried, with use of hyperventilation and/or sleep following sedation. Practically any variation of the EEG test is possible if requested by the referring physician. For example, if the doctor wishes an EEG study to be made in relationship to a glucose tolerance test,

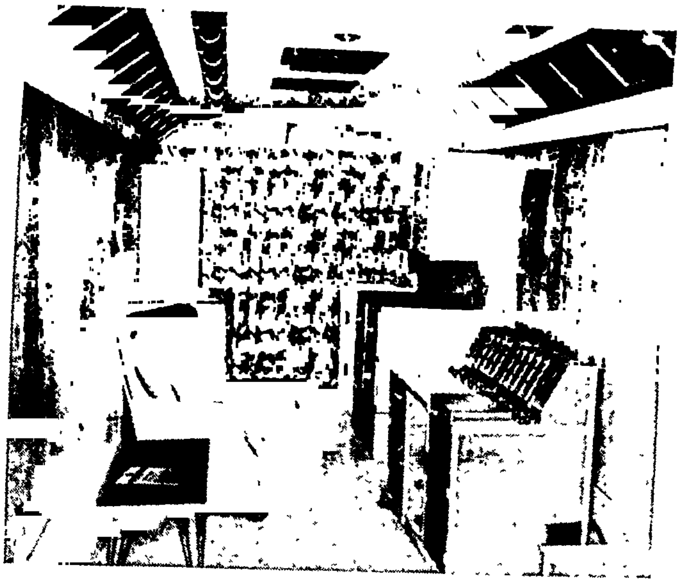
Fig. 2.—Inside of truck looking toward back from co-driver's seat. Curtain shuts off back windows. On right-hand wall are eight-channel electroencephalograph, cabinets for kitchenware above and clothes below, and combination sink, two-burner stove, and refrigerator. At left are chair used for patient during EEG, more storage cabinets, and clothes closet. By moving curtain into position behind EEG instrument, working and living quarters can be separated.

the blood tests can be done in the hospital laboratory concurrently with brief EEG tests of 10 minutes' duration once every hour.

All EEG records taken on the road are mailed to Detroit, where they are read by the neurophysiologist. This report is then given to the neurologist who, by this time, has a complete folder on each patient. It contains a statement from the referring physician relative to present medication, seizure occurrence, and particular problems of management. There is also available to the neurologist a birth record, a detailed history form filled out by patient or parent, and copies of reports from previous hospitalizations or specialized treatments.

From all of this material, the neurologist adds to the EEG report his diagnostic considerations and suggestions for the continued management of the patient. The referring physician therefore receives both the EEG report and neurological consultation. Of the 150 to 200 patients examined each summer, there are occasional problems which require more detailed study. In these instances, the neurologist recommends and offers the physician the further service of a neurological examination of the patient. Neurological clinics are then scheduled at central locations, where the referring physician, neurologist, and neurophysiologist have an opportunity to examine the patient together and to decide upon further procedures. What hospital or other facility he will choose to carry out these further recommendations is left to the discretion of the referring physician. Occasionally, these mobile services stimulate a county medical society to invite the center's staff to an evening meeting. The staff shares its extensive experiences in the field of epilepsy through the discussion of representative patient problems.

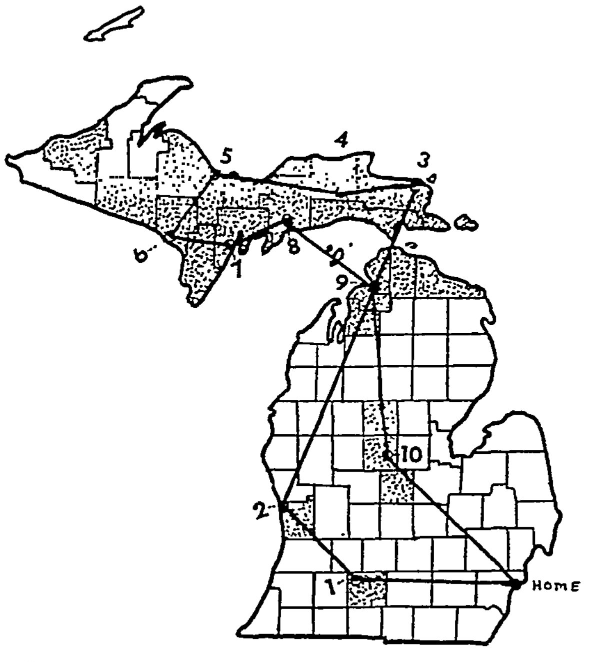

Fig. 3.—Route taken for summer of 1957. Counties serviced are stippled.

Relations of Center to Patients and Physicians.—The method by which this service reaches the patient and physician has been solved by a somewhat unique procedure. Through the counselors of the Michigan State Medical Society, the services are made known to each county medical society. Then, through any interested county medical society, we receive an invitation to bring the mobile service into its area. A letter is sent from the center to each member of the county medical society requesting service, inviting him to refer any of his patients suspected of having convulsions. Upon receipt of the doctor's referral, each patient is contacted, given a history form to fill out, and advised of the time, place, and date for the EEG study.

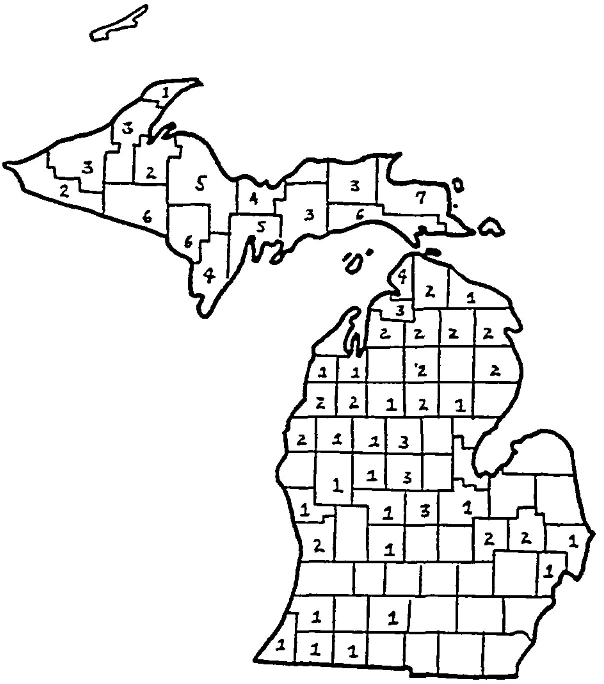

Fig. 4.—Counties covered, 1951-1957. Numerals show total number of visits to each county from 1954 through 1957. Areas without visits (*blank*) are serviced by stationary EEG laboratories. Most frequent visits are to Upper Peninsula area because it is furthest from stationary EEG facilities.

Administrative Aspects of the Program.—Selection of areas to be covered, contact with county medical societies, and contact with the referring physicians must be done months before the mobile unit begins its 10-week trip on the road. It is important that any group considering a mobile program like this be cognizant of all the planning and administrative procedures that accompany this prelude to the actual summer's trip.

The budget preparation and its justification to the Michigan United Fund are the responsibility of the executive director (R. D. Dennerll). A physician (H. B. Zemmer), as chairman of the statewide mobile committee of our board of directors assists in planning the areas to be covered. He also interprets to the officers of state and county societies the services of the mobile program. The voluminous correspondence and the creation of the precise route and schedule are the responsibility of one of us (A. L. R.) throughout the six months before the unit leaves Detroit (fig. 3). In planning a summer's route, we take account of the areas of first requests and areas covered during the last two years, as well as the probable needs of each community. It is desirable to cover all the areas of the state without EEG facilities at least once every three years and to cover them in such a way that the 10 weeks is neither overprogrammed nor underprogrammed.

Responsibility for the medical service rests with one of us (Z. S. B.) as the center's medical director. The education department at the MECA maintains from the inception to the completion of the program a liaison between the center and the communities being served through such mediums as newspapers and radio.

Summary of Mobile Unit Program

Yr.	Counties Served	M.D.s Contacted	M.D.s Referring	Patients Seen	Unit Stops	Mileage
1951........	11	182	53	95	8	1,329
1952........	17	90	31	96	5	1,007
1953........	17	82	34	71	5	682
1954........	26	396	57	175	8	1,184
1955........	20	203	60	150	8	1,281
1956........	14	341	49	123	8	1,301
1957........	21	399	72	190	10	1,271
Totals...		1,993	359	900	51	8,055
Averages per year.	18	285	51	129	8	1,151

An average of 18% of the doctors contacted referred about 2.5 patients each.

Results

Areas Covered.—In the seven years of mobile unit operation, 54 counties out of a total of 83 have received the service. After about two years, we found that particular localities, especially in the Upper Peninsula, were looking to the center for repeated EEG service. In fact, 12 out of the 15 counties (80%) in the Upper Peninsula have requested and received service for three or more years (fig. 4), compared to 5 out of 39 counties (13%) in the Lower Peninsula during the same seven-year period.

The table represents a summary of the number of counties serviced each year, the number of physicians invited to refer patients, the number who actually made referrals, the number of patients who received the examination, the number of stops made, and the distance the unit traveled. One important problem not revealed in the table is the problem of scheduling appointments and determining the number of days the unit must remain in any stop. It has been our experience that the anticipated number of patients scheduled often differs from the actual number referred, once the unit has arrived. In 1957, we anticipated 147 patients and were asked to see 190. The same summer, the number of physicians who indicated their intent to refer patients before the unit left Detroit was 48. However, the total number of referring physicians at the end of the summer was 72.

Financial Problems.—A charge of $30, which this year represents one-half of the total cost per capita, is asked of each patient with the request that he pay all, or as much as is possible, of this minimal charge. The other half of the cost, which is not asked of the patient, plus whatever part of the $30 he does not pay, is absorbed as part of the operating budget supplied by the Michigan United Fund. The patient is informed that it is the voluntary contributions of the people of Michigan through the Michigan United Fund that makes up this difference. The cost of the mobile program to the center, including prorated administrative expenses, was $12,270 in 1956 and an estimated $13,750 in 1957. Total reimbursement in patient fees was $1,877 in 1956 and $1,760 (to the time of writing) in 1957.

Comment

Implications of EEG Study.—A first concern was to determine if the EEG made in the mobile laboratory was equivalent to the routine EEG in quality. By inspection it appeared to be as free of confusing artifacts as any being currently taken in Detroit. The techniques, electrodes, and length of record were identical. Therefore, the differences and similarities are discovered by comparing the profile of frequency of occurrence of each rating for three sources of patients (comparison groups). These consist of (1) the records from the mobile program; (2) records from the Detroit laboratory of the MECA; and (3) records from a private, voluntary, nonprofit hospital (Harper Hospital). In figure 5A is shown the EEG ratings on a five-point scale[2] for the three comparison groups of records. All records were read and rated by the same person (A. J. D.); consequently we can compare the EEG ratings from the three sources. The pattern is the same. In fact, the curves for the traveling records and for those referred to a general hospital are almost identical. The patients sent to the center, however, show a greater number of more disturbed EEG patterns, while those at the private hospital show the least disturbance. To further understand these relations and to further evaluate the reliability of this comparison, the distribution of ages in five-year blocks was compared for these comparison groups. The number of patients found in each age group is expressed as a percentage of the total number of patients in each comparison group. This relationship is graphed in figure 5B. The per cent population at 5 to 9 years of age was arbitrarily chosen as the point at which the three distribution curves were made equal. This point was chosen because it tended to place the three curves most nearly together for less difficulty in comparison. The comparison brings out that all three distributions are similar between 5 and 34 years of age.

The greatest proportion of patients from 0 to 4 years of age is found in the Harper Hospital population because of its large pediatric ward and the many pediatricians on its staff. These 0-to-4-year-old patients are next most commonly found in referrals by general practitioners to the mobile unit. Since both the above groups are reluctant to consider the diagnosis of epilepsy until the patient is older, the center receives the lowest percentage of these patients (infants).

From 35 years of age and over, another deviation occurs. The patients of these older age groups are more commonly referred to the mobile unit and to the general hospital than to the center. This probably is the result of the generally held knowledge that in older patients the onset of seizures most likely is related to organic illness. The tendency, therefore, would be to send a patient in this age group to a neurologist or general hospital, and not to an epilepsy center. Like the general hospital, the mobile unit receives these cases because of the lack of specialists in neurosurgery and neurology in rural areas.

Implications of Traveling Program in Medical Practice and Doctor-Patient Relationships

Diagnostic Implications.—Inasmuch as all patients are referred to the mobile unit by their doctors and because we have the referring physician's material concerning the patient as well as records of his previous hospitalizations, we are in an excellent position to review the medical management prior to the time of the request for EEG and neurological consultation. We find, on the whole, a high degree of excellence of medical practice with convulsive disorders. These physicians use a wide variety of drugs and combination of drugs. The drugs are not always given up to maximum needs for seizure control, but seldom do we find cause to recommend use of different drugs. In some instances, our study may correct, or help clarify, the type of seizure that would necessitate the addition or change to a specific drug of choice for that particular type of seizure. Also, our experience may help the doctor focus treatment in areas other than medication, which also need consideration for seizure control.

Doctor-Patient Relationship.—It has been our experience that the very presence of this diagnostic laboratory in an area tends to strengthen the patient-doctor relationship in many instances. The doctor has something tangible to offer his patient. Too, he has the opportunity to review his patient's progress with the neurophysiologist and neurologist. The patient, in turn, may read of the unit's arrival and is rekindled with new hope so that he returns to his doctor after prolonged absence. In those counties visited in successive summers, we find a closer relationship between the doctor and his patient with seizures, both working toward better seizure control until another "repeat" EEG can be obtained. In this way the attitude of hopelessness, which stems from both the physician and the patient with uncontrolled convulsions, can be changed. Renewed interest and hope offers the opportunity for continued help, newer medications, and a stronger doctor-patient relationship.

Review of Therapeutic Progress.—Annual availability of modern instrumentation to the doctor and to his patients encourages repeated review of therapeutic progress and reduces postponed study. It has acquainted the physician with the use of EEG—its values and its weaknesses—in answering clinical questions. We are impressed that the same questions are behind the medical referral, regardless of the patient's location in the state: 1. Is this a convulsive disorder as I suspect? 2. Can this patient be taken off medication now that his seizures have been controlled for two years? 3. What kind of medication would help this patient? 4. Are there other factors, such as emotions or somatic disturbances, which contribute to this patient's seizure occurrence? 5. What capacity does this patient have for such aspects of living as school, marriage,

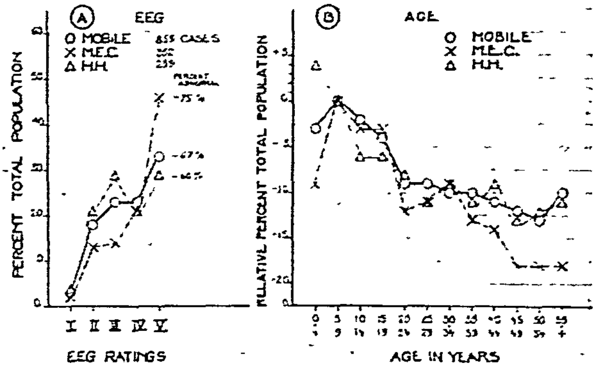

Fig. 5.—*A*, comparison of EEGs from three sources on basis of five-point rating. I=perfectly normal; II=normal; III=borderline normal and borderline abnormal; IV=abnormal; and V=diagnosably abnormal. H. H.=ratings of 239 consecutive cases referred to private hospital with diagnosis of possible convulsive disorder. M. E. C.=ratings of 352 consecutive cases referred to MECA in Detroit for full-team diagnostic examination. These patients have usually had diagnosis of convulsive disorder for some time. Mobile=ratings of 855 cases referred to mobile unit over last seven years. Percentage of abnormal patients gives proportion of patients rated V, IV, and III borderline abnormal. Values in percentage are placed opposite to end of curve representing those data. *B*, comparison of distribution of age of patients referred to three sources used in *A*. Percentages were all made equal at 5-to-9-year range and each plotted as differences from that value.

driving, and working? 6. What are the evidences for some organic disturbance from trauma, infection, or neoplasm as an underlying cause?

As a rule, the report from the center tends to increase the number of patients with "symptomatic" convulsive disorder, as against the essential, or "idiopathic," disorder. We have reduced medication in the well-controlled patients, but, in general, we tend to recommend continuing minimal doses for a longer period than the referring doctor often does. We rarely find reason to disagree with the referring physician's diagnosis.

We constantly attempt to increase the patient's functioning within the range of reality. In one location, 12 recommendations were made concerning seven patients directed toward expanding each patient's social and physical activities. Even with our limited studies, we do find inescapable evidence in 20% of these patients that disturbances in the emotions and in such somatic processes as sugar, water, and energy metabolism contribute to the problem. Both tests and treatment recommendations are suggested in these cases.

Comparison with Other Mobile Programs.—A comparison with other mobile clinics and health units shows significant differences. It is probable that others, like ourselves, have each developed special diagnostic, public relations, and physical features directed to the solution of a particular illness or problem. It has been of interest in reviewing other mobile services to note the differences in methods of transportation, that is, airplane,[3] boat,[4] and truck[5]; in service offered, that is, complete or partial treatment[6] or diagnostic[7] and preventive[8] medical service; and in administration and financing, that is, private,[9] hospital,[5b] government,[10] and voluntary.[11] In none of this extensive review of the literature has there been any previous publication describing a mobile clinic using a delicate EEG instrument. We know that early EEG amplifiers were transported from place to place by Gibbs[11a] in the mid-30's, later in World War II by Schwab,[12] and finally in the Korean war by Caveness.[13] Dr. Caveness had a mobile unit aboard ship.

In review of other mobile programs, we have found that many different methods have been used successfully to relate the mobile program to the local doctor and his patient. These are determined by the financial backing, the finances of the group serviced, and the available local medical facilities.

Implications of Program for Community and MECA

Long before the actual presence of the traveling unit in a community, its arrival is anticipated from agencies whose record pertaining to a patient has been requested by the Detroit center. These agencies then in turn look to the test results as supplementing their information and offering them assistance in their planning for the patient. These agencies are as numerous as they are wide in scope. They may represent the epileptics' interest in school, vocational training, eligibility for Old Age Survivors Insurance benefits, eligibility for guidance and counseling, a legal decision, and many other areas. Obviously, an EEG and neurological consultation cannot offer answers in all of these areas, nor can the report always present an adequate appraisal of the person's individual capabilities. It would be as unfair to use an EEG rating for the sole determination of a patient's capacities as it would be unfair to judge a person according to his IQ rating alone. We do feel that much more needs to be done in making our usefulness felt by social agencies in a community and in the same way gaining from them their particular kinds of information that would help us better to understand a patient's needs, his pressures, and, therefore, his seizures.

However, the problem of answering the many and varied questions raised by the local resources is not solved by mere exchange of information. This is the case whenever the limitation of getting information exists within the program itself. What answers we can give, plus repeated visits to some areas where the physicians have had opportunity to obtain an annual review of their patient's seizure activity demonstrated by EEG, has aroused interest within these communities for permanent facilities to provide a more complete evaluation of the patient. We are encouraged by this attitude and interest. It reflects again the need for studying the epileptic completely, as has been demonstrated for 10 years at the Detroit center.

It has been our experience that the number of referrals to the Detroit center for the complete physical-emotional-social diagnostic evaluation has increased within the areas visited by the mobile unit. Some patients and physicians have felt that the 200 or 300 miles traveled to Detroit is a negligible factor for the information necessary to plan adequately for a patient's treatment program. Again, it is a demonstration of the need for establishing permanent centers in those areas now alert to the value, as well as the limitations, of EEG and, more important, alert to the treatment possibilities now recognized for helping the epileptic.

Summary

Since 1951 the Michigan Epilepsy Center and Association (MECA) has had a mobile electroencephalography (EEG) laboratory. An eight-channel EEG instrument is mounted in a suitable truck and driven over 1,000 miles during a 10-week period each summer. Stops for the mobile unit are arranged prior to the date of departure, and areas visited are determined by invitation from the

county medical societies. EEG studies are made on appointment arranged with the patient at the request of his physician.

The EEG tracings are read by an electroencephalographer. Their accuracy is compared to those obtained at permanent installations at the MECA and at a private hospital. The neurologist at the MECA reviews the EEG readings, the patient's history, copies of previous medical reports, and data from the physician. A copy of the EEG report and the neurologist's suggestions pertaining to management are returned to the referring physician.

This paper describes the administrative problems, costs, geographical distribution of service, and a comparison with other mobile clinics. It discusses the implications of this program with regard to the doctor-patient relationship and to the community. The EEG mobile clinic makes available to an area with a widely scattered population and little concentration of resources this relatively expensive EEG instrument, trained personnel, and technical procedure.

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DIABETES IN THE AGED.—First, let me say a word about the incidence of diabetes and its detection at all ages. Approximately 1 per cent of the population has it, and another 1 per cent has it but does not know it. In the wards of hospitals in Boston which we recently surveyed, in a twelve-month period there were 500 patients with surgical lesions of the foot who proved to have diabetes. Ten per cent of them admitted no previous knowledge of the disease. The cost of that group of cases is tremendous, not merely in terms of dollar costs paid by the patient, but in terms of medical and surgical time. The diagnosis of diabetes is still a problem. A good test for sugar in the urine does not exist. With present procedures, a frank case of diabetes can be detected, but not a borderline case. We still are hampered by inadequacies of the fasting blood sugar method. In 1954, five hospitals in Boston tried the experiment of determining the blood sugar level of middle-aged patients without diabetes, one hour after breakfast. Five per cent of the first 300 patients had diabetes which was unrecognized and untreated simply because they had been tested previously by the fasting blood sugar method—which is sure to miss in some cases of diabetes.—Howard Root, M.D., Panel Discussion on Diabetes Mellitus in the Aged, *Journal of the American Geriatrics Society*, June, 1957.

CLINICAL NOTES

SIMPLE INSTRUMENT FOR EVALUATING PULMONARY VENTILATORY FUNCTION

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and
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The measurement of vital capacity alone is rarely adequate for estimating ventilatory function.[1] Several other tests, such as maximum breathing capacity and residual volume determinations, are often additionally employed in pulmonary function studies. The maximum breathing capacity test, though a dynamic pulmonary function test, has many shortcomings.[2] The apparatus is cumbersome, and the procedure is fatiguing to incapacitated patients. Other more elaborate pulmonary function tests usually require expensive equipment and skilled technical knowledge, and they are often time consuming. Such tests frequently require special facilities which are available in pulmonary research laboratories and not to the average practicing physician.[3]

By attaching a solenoid and an interval timer to the standard vital capacity spirometer,[4] Gaensler constructed a simple instrument for the measurement of both the total and the timed expiratory capacity from 1 to 10 seconds. The one-second expiratory capacity, expressed as per cent of predicted total vital capacity, was found to correlate very closely with the maximum breathing capacity similarly expressed.[1a] Segal and associates[5] described the use of a vital capacity timed interval ruler for the measurement of the timed expiratory capacity in conjunction with the Collins respirometer. Franklin and co-workers[2b] suggested the clinical use of tracings of forced expiration. Recently, Worton and Bedell[6] reported the use of a gas meter as a substitute for the spirometer for the measurement of vital capacity and maximum breathing capacity.

For evaluating bronchodilator drugs, Cander and Comroe[1b] introduced the use of maximum expiratory flow rate (MEFR) as a measurement of the expiratory resistance. They employed a Benedict Roth type of spirometer which was made to record on rapidly moving kymograph paper. The MEFR, expressed in liters per minute, was calculated from the time required for the expiration of 1 liter of air measured from the 200-cc. to the 1,200-cc. volume on the spirometer calibration curve. To achieve greater compactness and portability, Johnston and one of us (R. E. S.)[7] attached a synchronous timer and means for recording simultaneously the time and the angular displacement of the bellows of a McKesson-Scott vital capacity machine.

The present paper is concerned with an improved apparatus based on the same principle but offering greater convenience of operation and ease of computing MEFR, timed expiratory capacity, and total vital capacity. Construction detail, procedure for operation, method for computing measurements, and sample tracings are also presented.

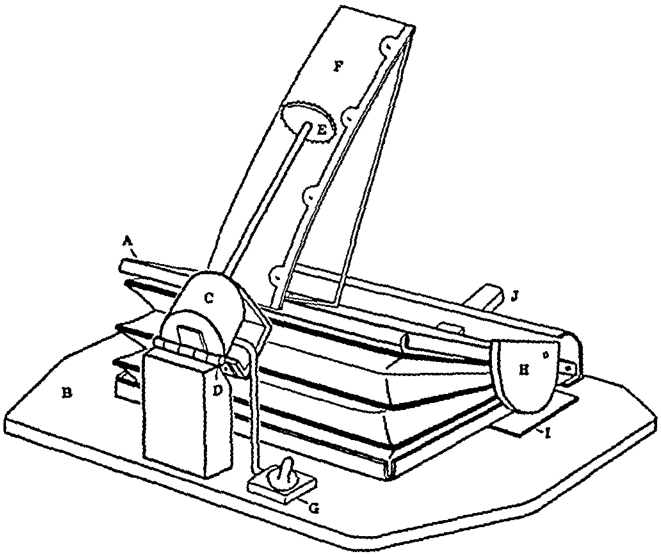

Fig. 1.—Recording spirometer apparatus, illustrated with bellows in partially inflated position. *A*, lid of McKesson-Scott vital capacity apparatus; *B*, flat board; *C*, clock; *D*, hinge; *E*, gear; *F*, supporting plate holding record strip; *G*, switch; *H*, cam; *I*, sandpaper; *J*, mouthpiece.

The Apparatus

Construction of Apparatus.—The design of the apparatus is aimed toward achieving the following features: (1) measurement of timed and total expiratory capacities and MEFR simultaneously and accurately after one single forced expiration; (2) inexpensive cost of construction, operation, and maintenance; (3) simplicity in conducting the test

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From the Lilly Laboratory for Clinical Research, Indianapolis General Hospital.

and computing results; and (4) permanent records of performance which may be included in patients' charts for later comparison.

The McKesson-Scott vital capacity apparatus is used as a receptacle for expired air and is supported by a flat board, at one end of which the recording assembly is mounted (fig. 1). The time-recording device consists of a synchronous clock motor, to the shaft of which is mounted a brass spur gear. The motor is mounted on a hinge so that the gear contacts the recording paper directly.

Pressure-sensitive recording paper is held on a curved aluminum supporting plate. As the motor shaft rotates, the gear teeth scratch lines on the pressure-sensitive paper. On each side of the hinged lid and pivotally mounted to it near the hinge is a spiral-shaped cam made of plywood. The cams serve as a "catch," holding the lid of the apparatus and the record strip at the position of maximum displacement. The motor rotates the gear once per second. The brass spur gear, originally with 30 teeth, has every sixth tooth removed with a file. Thus, with the gear rotating once per second, each tooth inscribes a line on the pressure-sensitive paper every 1/30 second and at intervals of every 1/5 second there is a wider space because of the absence of every sixth tooth.

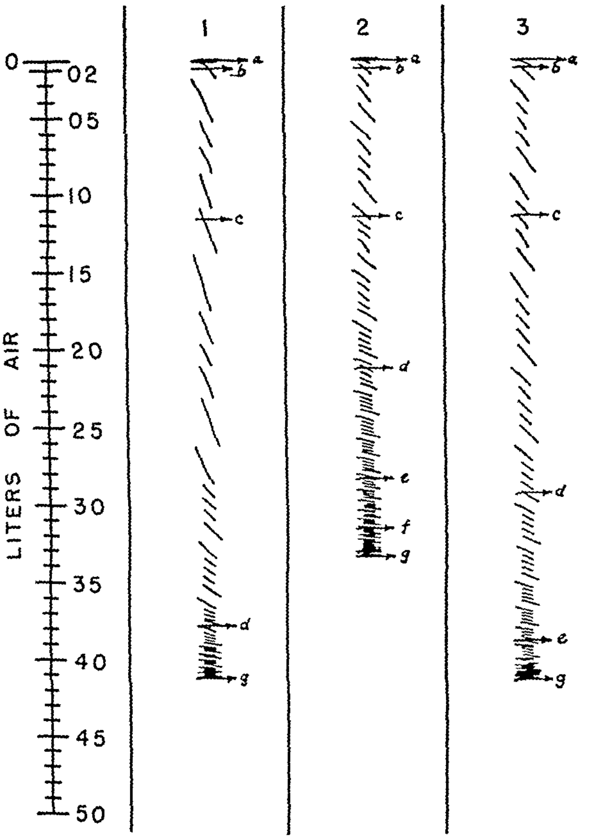

Fig 2.—Records illustrating method for measuring vital capacity, timed expiratory capacities, and maximum expiratory flow rate (MEFR) Volume calibration scale is on left. Tracings for (1) normal young man, (2) asymptomatic patient with bronchial asthma, (3) same patient 15 minutes after bronchodilator therapy, a = zero volume, b = 200-cc volume, c=1,200-cc volume, d=one-second capacity, e= two-second capacity, f = three-second capacity, g = vital capacity MEFR is computed from time elapsed between b and c (table 1) Values for MEFR in tracings 1, 2, and 3 are 333, 171, and 180 liters per minute respectively

Table 1.—*Maximum Expiratory Flow Rate (MEFR) in Liters per Minute Corresponding to the Number of Lines or Spaces*

Lines*				Spaces†			
No	MEFR	No.	MEFR	No	MEFR	No	MEFR
1	1,800	11½	156	1	300	11½	26
1½	1,190	12	150	1½	198	12	25
2	900	12½	144	2	150	12½	24
2½	720	13	138	2½	120	13	23
3	600	13½	134	3	100	13½	22.3
3½	515	14	128	3½	86	14	21.4
4	450	14½	123	4	75	14½	20.6
4½	402	15	120	4½	67	15	20
5	360	15½	116	5	60	15½	19.3
5½	333	16	112	5½	55.5	16	18.7
6	300	16½	109	6	50	17	17.6
6½	276	17	106	6½	46	18	16.6
7	258	17½	103	7	43	19	15.8
7½	240	18	100	7½	40	20	15
8	225	18½	97	8	37.5	22	13.5
8½	210	19	94.5	8½	35	24	12.5
9	198	19½	92.3	9	33	26	11.5
9½	189	20	90	9½	31.6	28	10.7
10	180	21	85.7	10	30	30	10.0
10½	171	22	81.8	10½	28.5	32	9.3
11	162	23	78.2	11	27	34	8.8

* Interval between two lines = 1/30 second
† Interval between two wider spaces = 1/5 second

Calibration of the Apparatus.—After the apparatus has been assembled, it is calibrated as follows. The rubber inlet tube is attached via an adapter and a three-way stopcock to a 50-cc. syringe. The pressure-sensitive paper is placed on the supporting plate. The gear is then placed in contact with the paper, and the motor is turned on at the switch. Approximately 150 cc. of air must be introduced before any displacement of the lid will be observed. Pressure within the rubber bellows is 1.2 cm. H_2O at 1.0 liter displacement and 4.0 cm. at 5.0 liters. The volume displacement is recorded on the paper as a horizontal line for each 50 cc. of air injected. The calibration recorded on the paper is then transferred to a transparent plastic strip and is used for the measurement of vital capacity, timed expiratory capacities, and MEFR.

Test Procedure and Results

Test Procedure.—The operator attaches the pressure-sensitive paper to the supporting plate and places the motor assembly in the position which permits the gear to contact the recording paper. A disposable paperboard mouthpiece is then inserted into the rubber outlet. The test may be conducted with the patient in either the standing or sitting position.

Instruction to the Patient.—The patient is carefully instructed by the operator to inhale as deeply as possible and then exhale as rapidly, as forcefully, and as completely as he can into the mouthpiece. The patient is also told to avoid permitting air to pass through the nose or outside of the mouthpiece. The motor is turned on and the record made.

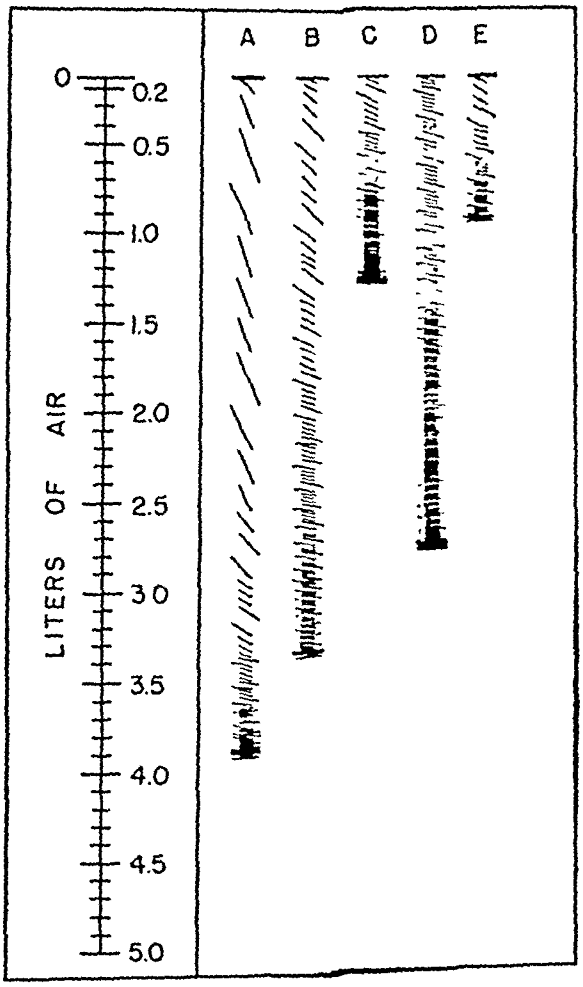

Fig. 3.—Records illustrating pulmonary insufficiency of different etiologies. *A*, normal young man; *B*, asymptomatic patient with bronchial asthma; *C*, asthmatic patient in paroxysm of moderate severity; *D*, patient with uncomplicated pulmonary emphysema; *E*, patient who had right pneumonectomy.

Computing the Results.—After the patient has completed the forced expiration, the motor is turned off, the record (fig. 2) is removed, and measurements are made as follows: The zero volume line on the plastic ruler is placed so as to superimpose the zero position on the record. The vital capacity of the patient is measured by reading on the plastic calibration strip the volume of the air at the position opposite the furthermost recorded line. The one-second expiratory capacity is obtained by starting at the zero point on the record strip and counting either five wider spaces or 30 lines. The position of this distance on the calibration strip gives the volume of air in liters expired during the first one-second of expiration. The two-second and three-second expiratory capacities are obtained in similar fashion by counting from the zero point to the 10th or the 15th wider space respectively.

As originally defined by Cander and Comroe,[1b] MEFR is determined by measuring the time required for the expiration of the one liter of air from the 200-cc. to the 1,200-cc. volume, as indicated on the calibration strip. This is most readily accomplished by drawing a line across the record at the 200-cc. and 1,200-cc. volumes, counting the number of 1/30-second marks to the nearest half, and then referring to a prepared table of values relating elapsed time to the corresponding MEFR in liters per minute (table 1). When one is measuring the intervals by counting marks, it should be remembered that the wider space occurring every 1/5 second represents an interval of time equal to two smaller spaces or a total of 2/30 second. For records from patients who have marked ventilatory impairment, it is more convenient to count the number of wider spaces and obtain the corresponding MEFR in liters per minute from the space column in table 1. Examples of the measurement of vital capacity, timed expiratory capacities, and MEFR are presented in figure 2.

Comment

Most disorders, whether primary or secondary, that diffusely affect the lung produce important changes in the ability of a patient to exhale forcibly.[2b] The method herein described provides means for measuring the extent to which the time-volume relationship in a single maximal expiration reflects alterations in ventilatory function. Additional information can be obtained from more elaborate ventilatory tests, but their clinical usefulness is hampered by the necessarily complicated apparatus and time-consuming procedure.

It is of interest that distinguishable patterns are identifiable in records from patients with ventilatory insufficiencies having different etiologies (fig. 3). In the average normal adult, 70 to 90% of

Table 2.—*Vital Capacity, Maximum Expiratory Flow Rate (MEFR), and Timed Expiratory Capacities Computed from Tracings in Figure 3*

	Subject				
	A	B	C	D	E
Vital capacity, liters	4.00	3.40	1.35	2.90	1.00
% of Normal*	99	82	52	69	24
MEFR liters per minute	360	138	20	40	..
½-sec. capacity,† liters	2.90	1.22	0.60	0.50	0.70
1-sec. capacity, liters	3.55	2.00	0.85	0.85	0.90
2-sec. capacity, liters	3.87	2.65	1.06	1.40	..
3-sec. capacity, liters	..	3.05	1.20	1.70	..

* Based on height, age, and measured vital capacity of each patient (Baldwin and others: Medicine 27:243-278 [Sept.] 1948).

† One-half-second expiratory capacity test (Miller and others: Dis. Chest 30:33-42 [July] 1956).

the vital capacity is accounted for within the first one-second capacity. MEFR in such individuals ranges from 350 to 500 liters of air per minute. During an asymptomatic period in patients with bronchial asthma, the general pattern of the expiratory record grossly resembles the normal tracing; however, when an effective bronchodilator is given, the patient's vital capacity, timed capacities, and MEFR show definite improvement (fig. 2), whereas no consistent changes were observable in this study after similar medication in normal individuals. In this way patients with bronchial asthma having subclinical impairment could be differentiated from normal individuals. In patients having acute paroxysms, the record pattern (fig. 3*C*) shows the vital capacity, timed capacities, and MEFR to be greatly but quite proportionally reduced. In the case of uncomplicated pulmonary emphysema, the vital capacity is reduced but proportionately much less so than the markedly reduced time capacities and MEFR (fig. 3*D*). In patients who have had pneumonectomy, the reduction of vital capacity is greater than the reduction of timed capacities and MEFR. The record pattern as shown in figure 3*E* is characteristic of restrictive pulmonary insufficiency. Thus, a patient's expiratory performance may often be appraised with reasonable accuracy by simple inspection of an expiratory tracing (fig. 3).

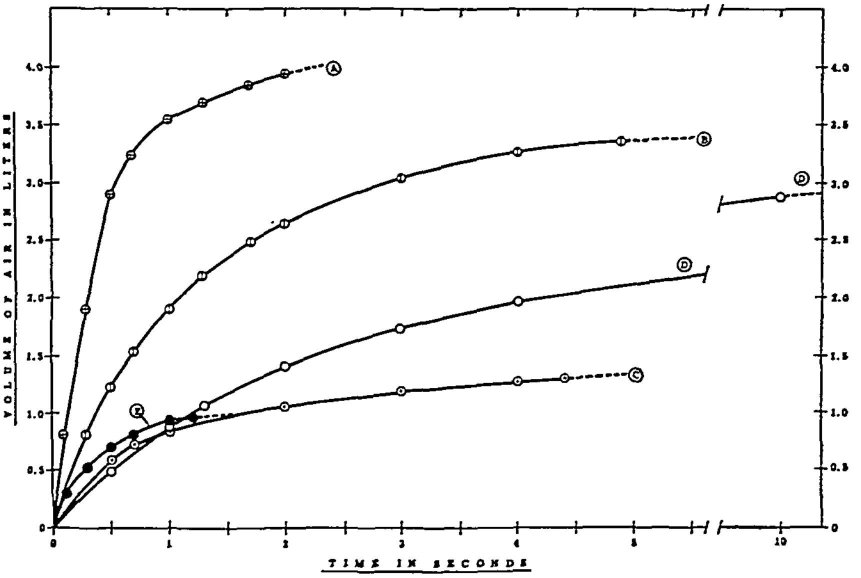

Fig. 4.—Graphic representation of figure 3, illustrating different expiratory tracings of patients with impairment of different etiologies.

For precise evaluation of and for estimating small changes in serial comparative studies, accurate computation should be made from the tracings. By plotting the expiratory capacities in liters of air against time in seconds obtained from the records of figure 3, an additional graphic representation of the different expiratory tracings is illustrated in figure 4. The vital capacities, MEFR, and timed expiratory capacities of the tracings in figure 3 are summarized in table 2.

Summary

A simple, inexpensive instrument, capable of measuring vital capacity, timed expiratory capacities, and maximum expiratory flow rate simultaneously and accurately during a single forced expiration may provide permanent records of performance which may be included in a patient's chart for later comparison. The instrument is compact and portable and can be conveniently used in the ward, clinic, or office.

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Mr. Clifford Wilson provided technical assistance in this study.

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ACUTE MESENTERIC VENOUS THROMBOSIS SIMULATING ACUTE PANCREATITIS

THE VALUE OF PERITONEAL FLUID ANALYSIS

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and
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The clinical diagnosis of mesenteric venous thrombosis is often difficult to establish. The following case was incorrectly diagnosed as acute pancreatitis. Several diagnostic peritoneal taps were done during the patient's hospitalization, and in retrospect the gross findings and elevated amylase levels were more suggestive of mesenteric thrombosis than of acute pancreatitis. We hope that this case report will encourage the more widespread use of peritoneal tap as a diagnostic adjunct in cases of obscure abdominal disease.

Report of a Case

At his first admission to the Peter Bent Brigham Hospital, a 63-year-old man had the chief complaint of abdominal pain of two days' duration. Three weeks prior to admission the patient first noted mild constipation, which responded to laxatives and cathartics; three days prior to admission he gradually developed steady periumbilical and lower abdominal pain, which radiated to the middle part of the back. There were occasional cramp-like exacerbations of the pain. One day prior to admission the pain became more severe and was accompanied by vomiting. His last bowel movement, two days before hospitalization, was said to have been brownish-black in color. He had passed no gas per rectum after that. There had been no previous similar episodes of pain, and his general health had always been excellent. He had gained 5 lb. (2.3 kg.) in the past year. During the past several years he had had occasional episodes of postprandial indigestion and periumbilical pain relieved by Alka-Seltzer.

Physical Examination.—On physical examination, his temperature was 97.6 F (36.4 C), pulse rate 110 per minute, respiration 28 per minute, and blood pressure 90/50 mm. Hg. He was a well-developed, obese man obviously in acute distress. His skin was cold and moist, his pulse was rapid and thready, and his respiration was somewhat labored. The heart was slightly enlarged, with normal sinus rhythm and no murmurs; the lungs were clear on percussion and auscultation. Examination of the abdomen showed generalized board-like rigidity with diffuse tenderness and rebound. The tenderness seemed maximal in the right lower quadrant, there was moderate distension, and peristalsis was absent. On rectal examination, the prostate was normal and there was diffuse tenderness in the cul-de-sac but no mass.

Laboratory Studies.—The patient's hematocrit value was 61% on admission, falling to 46% on the second hospital day and 40% on the ninth. The white blood cell count was 27,000 per cubic millimeter, with 88% polymorphonuclear cells; this fell to 13,000 on the second hospital day and to 8,500 on the third. Findings on urinalysis were negative. The serum amylase level was zero Somogyi units on admission; it remained so for three days and then gradually rose to 164 on the sixth hospital day. The peritoneal fluid obtained shortly after admission was reddish-brown in color, with a mild fecal odor. The peritoneal fluid amylase level was 1,690 Somogyi units. No Gram's stain was done. The culture revealed Escherichia cóli. The peritoneal fluid amylase level dropped to 300 on the second hospital day and to 30 on the sixth.

X-ray Reports.—X-ray of the chest showed the lung fields to be clear, and that of the abdomen showed that there was no free air beneath the diaphragm. There were several nondilated, gas-filled loops in the small intestine with fluid levels in the left upper quadrant. There were, in addition, several radiopaque gallstones in the right upper quadrant. The roentgenogram of the abdomen on the fourth hospital day revealed only a minimal amount of gas scattered throughout the small intestine. The left psoas line was obliterated.

Hospital Course.—The patient was brought out of shock with a rapid infusion of 500 cc. of dextran, 900 cc. of plasma, and 500 cc. of whole blood. It was the feeling of the surgeon that the diagnosis of acute hemorrhagic pancreatitis, although not definitely established, best explained the clinical picture. Exploratory laparotomy to rule out perforated ulcer or intestinal infarction was scheduled four hours after admission, but it was cancelled when his blood pressure became unobtainable during the induction of anesthesia. He was then treated with penicillin, streptomycin, and suction with a Levin tube. Therapy with 300 mg. per day of hydrocortisone, given intravenously, was begun on the second hospital day and continued for a week; then the dosage was gradually tapered down. His temperature on the second hospital day rose to 103 F (39.4 C) and spiked to 102 F (39 C) each day thereafter. On the third hospital day he was noted to have some edema and erythema of the flanks, more marked on the left. From the fifth hospital day on, his abdomen became softer and less tender and his general condition appeared slightly improved. On the 10th hospital day he suddenly developed marked difficulty in breathing, and he died while emergency bronchoscopy was being performed. Bronchoscopy revealed that a large, firm, mucus plug had obstructed the glottis.

Postmortem Examination.—The body was that of a well-developed, slightly obese, elderly male, with a distended abdomen. The laryngeal mucosa was slightly swollen and was covered by thick, adherent yellow mucus and by some gastric contents. An abundant amount of tenacious, purulent mucus filled the tracheobronchial tree, the mucosa of which was markedly congested. Each lung weighed 620 Gm., and both were large and firm, with a markedly congested parenchyma which contained numerous small portions of collapsed alveoli. The heart was unremarkable. The peritoneal serosa was covered by a layer of fibrinous exudate, which matted together the intestinal loops. Between these matted loops were loculated cavities which contained a total of 500 cc. of brown, turbid, foul-smelling, fetid fluid. All of the small intestine was dilated, and the serosa had a purple-red color. These changes were most accentuated in a 20-cm. segment of ileum, which was frankly infarcted, with a blue-red wall thickened by hemorrhage. The distal limit of the infarcted segment was 25 cm. proximal to the ileocecal

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valve. The blood vessels of the ascending colon were engorged with blood, but the wall of the whole colon appeared otherwise unremarkable. At the inferior border of the pancreas, the superior and inferior mesenteric veins joined to form a common mesenteric vein. The lumen of this common mesenteric vein was completely occluded by an adherent, gray-red, laminated thrombus. Likewise, all of the superior mesenteric venous tributaries were filled by dark red, firm thrombi. The splenic and portal veins and the mesenteric arteries were free of thrombi. Benzidine-positive liquid fecal matter was found within the stomach and small intestine.

Microscopic Examination.—Microscopic examination of the lung revealed all the lobes acutely congested, with foci of intra-alveolar extravasated erythrocytes in the upper lobes and large portions of collapsed and airless parenchyma in the lower lobes. On examination of the jejunum, moderate numbers of polymorphonuclear leukocytes and engorged blood vessels were seen between the normal-appearing elements of the wall. On the serosal surface there were large masses of neutrophils embedded in meshes of fibrin. Within the subserosal veins recent thrombi were found partially adherent to the intima. Examination of the ileum revealed that the normal cellular detail of the infarcted segment was lost; this was due to necrosis of the wall, which was infiltrated by abundant extravasated blood, bacterial colonies, and foci of cocci. The subserous veins contained recent thrombi, and their walls were infiltrated by neutrophilic leukocytes and scant bacteria. The cecum was unremarkable, except for capillary congestion and thrombosis of the subserous veins. Within the mesenteric vein wall were clumps of histiocytes, monocytes, and polymorphonuclear leukocytes. Attached to the intima was a recent thrombus, whose periphery was being invaded by numerous capillaries. The pancreas and liver were unremarkable, and the remainder of the gross and microscopic examinations was noncontributory.

In summary, the autopsy disclosed extensive thrombosis of the common mesenteric vein and of the trunk and radicles of the superior mesenteric vein. A 20-cm. segment of ileum was necrotic and had produced diffuse peritonitis. There was no evidence of pancreatitis. Since the mesenteric venous thrombosis was not secondary to any abdominal disease process, this case falls within the group described as agnogenic mesenteric venous thrombosis.[1]

Comment

The significant peritoneal fluid findings in this case, which suggest intestinal infarction rather than pancreatitis, are (1) the cloudy, reddish-brown appearance, (2) the mild fecal odor, (3) the positive culture of Esch. coli, and (4) the amylase level of 1,690 Somogyi units.

An unusual feature of this case was the persistently low serum amylase level (zero on three occasions). It has been stated that a serum amylase level of zero is indicative of massive pancreatic necrosis.[2] At autopsy, however, the pancreas was perfectly normal. It is conceivable that the thrombosis of the portal system prevented normal absorption of pancreatic amylase, resulting in the low serum levels.

We are convinced of the value of peritoneal tap in the diagnosis of obscure abdominal conditions. The technique is simple and has not resulted in complications in our personal experience or in the experience of others, as gathered from a review of the literature. We have been using a no. 20 short bevel intravenous or spinal needle in any or all examinations of the mid-lateral quadrant. Neuhof and Cohen,[3] in a series of more than 100 taps, did not observe a single instance of injury to the intestine. Thompson and Brown[4] reported 300 abdominal taps done at Charity Hospital in New Orleans without complication. Moretz and Erickson[5] reported eight instances in which the needle entered the lumen of the small or large intestine in a series of 161 diagnostic taps. In none of these patients could the puncture site in the intestinal wall or evidence of leakage be found on subsequent laparotomy. These workers also did experimental work on needle puncture of the small intestine in dogs.[6] Insertion of a no. 20 needle into dilated loops of small intestine with an intraluminal pressure of 100 mm. Hg resulted in no leakage of gastrointestinal contents after the needle was removed.

It is interesting that they reported an error in diagnosis[6] very similar to that in this case. A patient with a peritoneal fluid amylase level 11.3 times the normal serum amylase content was mistakenly given the diagnosis of pancreatitis. At autopsy, a strangulated gangrenous loop of jejunum was found involved in an internal hernia. The peritoneal fluid, much like that observed in our case, was reddish-brown in color and had a slightly fecal odor. Numerous white blood cells and gram-negative bacilli were seen on a direct smear.

Keith and co-workers[7] have shown that an elevated peritoneal fluid amylase level is helpful in making a diagnosis of acute pancreatitis. The elevation is often more pronounced (averaging 400-1,000 Somogyi units) and lasts two to four days longer in the peritoneal fluid than in the blood. Karlan and Zollinger[8] have noted an elevation of peritoneal fluid amylase level from 800-2,000 units in four out of six cases of mesenteric venous thrombosis in which peritoneal taps were performed. Ellison[9] has stated that, in his personal experience, elevation of the peritoneal fluid amylase level above 1,000 units is strongly suggestive of a necrotic intestine rather than pancreatitis. The mechanism of elevation of peritoneal fluid amylase level with infarcted intestine is presumed to be leakage of intraluminal enzyme through the abnormally permeable intestinal wall.

A Gram stain of the peritoneal fluid is probably the best way to differentiate pancreatitis from infarction of the intestine. In most of the cases of pancreatitis reported in the literature, smear of the peritoneal fluid, although containing many white blood cells, revealed no bacteria. Patients with intestinal infarction characteristically show both white bood cells and gram-negative bacilli on direct smear. Experimental work on dogs by Hill and co-workers[10] revealed that numerous gram-negative bacilli are found on peritoneal fluid smear within four hours of establishing infarction of the intestine.

Summary

Peritoneal tap is a safe and valuable diagnostic maneuver. The gross appearance, odor, and direct Gram-stained smear will serve to differentiate many intra-abdominal diseases. Elevation of peritoneal fluid amylase level above 1,000 Somogyi units, associated with gram-negative bacilli on smear, is strongly suggestive of intestinal infarction.

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ACUTE TUBULAR NECROSIS AFTER TRANSFUSION REACTION DUE TO ANTI-KELL ANTIBODIES

REPORT OF A CASE AND DISCUSSION OF MANAGEMENT

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The pathophysiological alterations in the kidneys of previously healthy individuals who suddenly develop oliguria or anuria have recently been more clearly elucidated. In 1942, Bywaters[1] described the clinical and pathological features of the crush syndrome. Lucke[2] reported that similar ischemic lesions of the tubules could result from several etiological factors and suggested the term lower nephron nephrosis. Oliver,[3] however, demonstrated that the terminal part of the proximal convoluted tubule is involved as often as the distal tubule. Such cases of acute renal failure continue to be described as lower nephron nephrosis, but the syndrome is more appropriately termed acute tubular necrosis.

Numerous etiological factors may produce this syndrome. However, transfusion reactions continue to be one of the most frequent causes. The present report describes a patient who developed acute renal insufficiency after an incompatible blood transfusion due to anti-Kell antibodies but in whom the usual manifestations of a hemolytic reaction were not observed.

A 37-year-old housewife was referred to Duke Hospital on July 20, 1956, for evaluation and management of anuria of 72 hours' duration. Three days prior to transfer to Duke Hospital she had been admitted to a local hospital for an elective repair of an umbilical hernia and a cystocele and for a diagnostic dilatation and curettage. The hemoglobin level on admission was 11.8 Gm. %. She was given one unit of blood which was considered compatible by the saline cross matching technique. During the third hour of the transfusion, the patient developed chills and urticaria and, one hour after the transfusion was terminated, a temperature of 40 C (104 F), severe vomiting, and diarrhea.

The following morning (July 18), the patient allegedly voided 240 ml. of clear, yellow urine. The vomiting and diarrhea persisted and she received 1,000 ml. of 5% dextrose in water and 1,000 ml. of 5% dextrose in saline solution. As she did not void again, she was catheterized approximately 42 hours after the transfusion. Only 15 ml. of urine was obtained; it was reported to be clear, of yellow color, and completely normal. The nonprotein nitrogen level at that time was 79 mg. %. The icteric index was normal.

On July 19, because of continued vomiting, bloody diarrhea, and fever (38.3 C [100.9 F]), the patient received fluids intravenously, including 1,000 ml. of dextrose in saline solution, 500 ml. of Polysal (a balanced electrolyte solution containing, in milliequivalents per liter: sodium, 140; chloride, 103; carbonate, 55; potassium, 10; calcium, 5; magnesium, 3) in 5% dextrose, and 1,500 ml. of dextrose in water. Parenteral injections of chlorpromazine (Thorazine) hydrochloride, diphenhydramine (Benadryl) hydrochloride,

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dimenhydrinate (Dramamine), pyridoxine, and a variety of barbiturates were given. The anuria persisted and the patient was transferred to Duke Hospital.

The history was significant in that the patient previously had received three blood transfusions without reaction, the last being six months prior to this admission, for menorrhagia. She had had five pregnancies without toxemia, edema, hypertension, known albuminuria, or any other indication of renal disease. None of her pregnancies had resulted in erythroblastosis fetalis.

The physical examination revealed a pale, acutely ill patient, lying quietly in bed. She was conscious and cooperative, but complained of severe nausea. The temperature was 37.2 C (99 F), pulse 72 per minute and regular, respiration 16 per minute, and blood pressure 120/80 mm. Hg. Pertinent physical findings included slight periorbital edema; several small ecchymotic areas on the legs and arms; two flame-shaped hemorrhages in the left sclera. The sclerae were not icteric. The neck veins were distended at 45 degrees. The heart and lungs were normal save for an accentuated pulmonic second sound. A moderately tender liver edge was palpable three fingerbreadths below the right costal margin. The spleen was not palpable. The bowel sounds were hyperactive. There was no presacral or ankle edema.

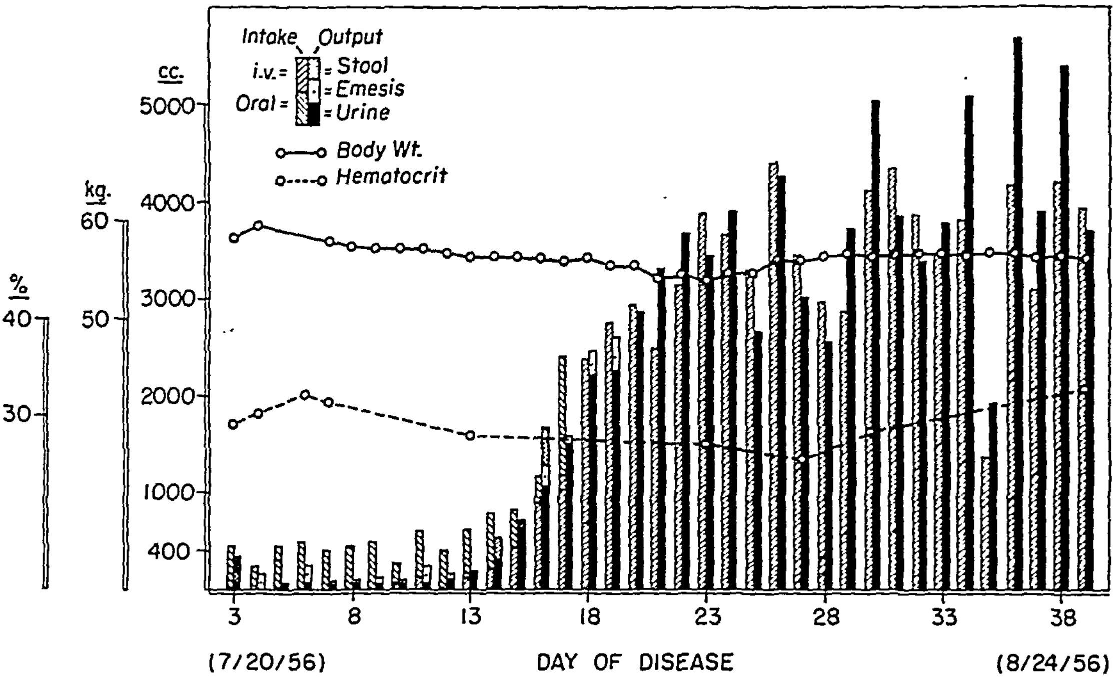

Fig. 1.—Fluid balance, body weight, and hematocrit during oliguric and diuretic period of acute tubular necrosis.

Laboratory Findings.—The laboratory findings were as follows: hemoglobin level, 8.6 Gm. %; hematocrit, 30%; red blood cell count, 3,840,000 per cubic millimeter; reticulocytes, 2.3%; mean corpuscular hemoglobin, 22.3 micromicrograms; mean corpuscular volume, 78.5 cu. μ; white blood cell count, 6,750 per cubic millimeter with a normal differential; platelets adequate. Sedimentation rate, levels of bilirubin, amylase, and total protein, and albumin:globulin ratio were normal. Serologic tests for syphilis were negative. Serum electrolytes (milliequivalents per liter): sodium, 141.3; potassium, 4.0; chloride, 101.2; carbon dioxide, 19.2. Nonprotein nitrogen level was 81 mg. %. Reaction to the Guaiac test was positive; culture was negative for pathogens. The patient was unable to void but was not catheterized. The agglutination tests for typhoid, paratyphoid A and B, and tularemia were negative. The electrocardiogram was normal. Blood cultures were negative.

Diagnosis.—It was apparent on the day of admission that the patient was in acute renal failure, as evidenced by elevation of level of nonprotein nitrogen, acidosis, and complete anuria. There was no evidence to suggest an obstruction or a preexisting renal lesion. The bleeding tendency was thought to be related to acute uremia. The hepatomegaly, neck vein distention, and an accentuated pulmonic second sound suggested early congestive heart failure. The temporal relationship of the blood transfusion and the onset of symptoms was thought significant.

Hospital Course.—The patient remained oliguric for 14 days. In this clinic, a urine output of less than 400 ml. per 24 hours by a patient on a normal diet is defined as oliguria. This is the minimal volume necessary to prevent progressive azotemia. The spleen became palpable on the third day of observation. By the fifth day, the neck vein distention and hepatosplenomegaly had disappeared. The bloody diarrhea subsided on the fourth day. The blood pressure and temperature remained normal during the entire observation.

Details of the fluid balance, body weight, and hematocrit are recorded in figure 1. The nonprotein nitrogen level and serum electrolytes, including calcium and phosphorus, are shown in figure 2. Figure 3 lists urine electrolytes in regard to concentration and 24-hour excretion. Arterial pH values on the 11th, 13th, and 16th day of the illness were 7.25, 7.24, and 7.26 respectively. Osmolarity determinations of the plasma and urine were 333.4 and 339 milliosmoles (mOsm.) per liter on the 12th and 329.2 and 325.6 mOsm. per liter on the 16th day of illness. Diuresis began on the 15th day. The electrocardiogram was normal on admission. Electrocardiograms were taken daily and on the eighth day of illness (July 25) changes suggestive of hyperkalemia (peaking of the T waves) appeared. Subjectively, the patient remained fairly cheerful and alert throughout the entire period of observation. Daily vomiting of small volumes for the first 17 days and occasional headaches constituted her only complaints.

Treatment.—The management of this patient was conservative. It consisted of bed rest, administration of antibiotics, respiratory isolation, and administration of 450 ml. daily of 30 to 40% dextrose with insulin (1 unit per 3 Gm.

of dextrose) and 10 mg. of heparin through a femoral catheter passed into the inferior vena cava. Nothing was given by mouth for the first 10 days. No electrolytes were given during this period.

When electrocardiographic changes suggesting hyperkalemia appeared, 10 cc. of calcium gluconate was added to the daily infusion. Testosterone propionate was injected for four days, 50 mg. intramuscularly every six hours. With the onset of diuresis, fluid was given in amounts matching the total output of the previous 24 hours. Oral feeding, at first low in protein and potassium, was begun, reaching a normal diet ad libitum on the fourth day of diuresis. Salt was also allowed ad libitum, and an additional 5 Gm. for two days and 10 Gm. for the third day was given intravenously. Sedatives, previously avoided, were now administered when needed, and multivitamin preparations and ferrous sulfate were added. Strict bed rest was abandoned after the fifth day of diuresis and the patient gradually became ambulant. She was discharged on Aug. 26, 1956, the 38th hospital day.

Follow-up.—The patient returned for checkups on Oct. 3, 1956, and Feb. 22, 1957, and was seen again in October, 1957. She continued to do well, subjectively and objectively, and was clinically asymptomatic. The urine was normal except for low specific gravity. The phenolsulphonphthalein excretion in two hours, which had been 11% on Aug. 10, 1956, and 13% on Aug. 15, was 48% on Oct. 3 and 69% on Feb. 22, 1957.

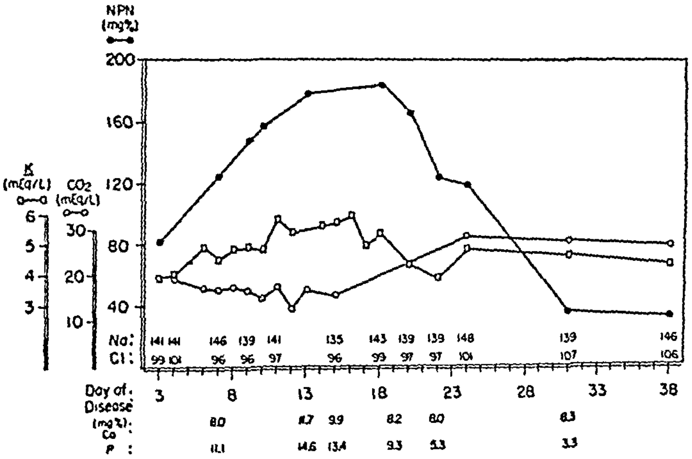

Fig. 2.—Nonprotein nitrogen level and serum electrolytes during oliguric and diuretic period of acute tubular necrosis.

Etiology

The acute renal failure developed immediately after a blood transfusion. Clinically, the patient apparently did not have the common type of hemolytic transfusion reaction; hemoglobinemia, icterus, or hemoglobinuria were not observed. Bloody diarrhea was a prominent feature. A number of other factors in the immediate history and in the presenting condition of the patient could be linked etiologically with an acute renal shutdown, such as bloody diarrhea with high fever, gastroenteritis in the family, and severe abdominal pain as possible indication of an abdominal emergency. The temporal relation to the transfusion, however, was very suspicious. The possibility that the patient might have received blood containing Gram-negative saprophytes, some of which are known to grow in refrigerated blood,[4] was rejected because of the absence of the typical reactions, particularly of profound shock with cutaneous hyperemia.

The diagnosis was obvious when it was found that the patient's red blood cells were Kell negative (kk), that her serum contained extremely potent anti-Kell antibodies, and that a blood sample received from the donor was Kell positive. The donor's cells were strongly agglutinated by the patient's serum when tested by the indirect Coombs' cross matching procedure, but, as is usual with these antibodies, gave a negative reaction when tested by the simple saline cross matching test. A direct Coombs' test of the patient's blood failed to reveal any of the incompatible donor cells in her circulating blood. The blood of the husband and children was also grouped as Kell negative (kk). Therefore, the patient's anti-Kell antibodies were undoubtedly provoked by her previous transfusions and not through her pregnancies.

Excluding the D (Rh_0) factor of the Rh system of blood groups, the Kell (K) factor is perhaps one of the most potent of the lesser antigenic blood group factors.[5] Sensitization of a K-negative woman by K-positive fetus fathered by a K-positive man with resulting erythroblastosis fetalis is not uncommon. Sensitization of either K-negative men or women by transfusion of K-positive blood is relatively frequent after multiple transfusions. Fortunately, only 10% of random white donors are K-positive,[5b] thus there is a 9:1 chance of compatibility with the blood of whites (50:1 with Negroes) if the antibody was undetected by the cross match. Unfortunately, the anti-Kell antibody, as in this case, is most often detected only by the Coombs' antiglobulin cross matching procedure. This fact emphasizes the necessity of employing the indirect Coombs' cross matching test for all transfusions, particularly for patients who give a history of previous transfusions or pregnancies.

Inasmuch as no evidence was observed in this patient of the usual rapid intravascular hemolysis any time after the transfusion, it is presumed the incompatible cells were rapidly removed by erythrophagocytosis. The demonstration of extremely potent anti-K antibodies in the patient's blood reacting strongly with the donor cells explains fully the pathogenesis of her disease. This case represents another confirmation for the fact that Kell antibodies are of considerable clinical importance as a cause of transfusion reactions. At the time of this patient's hospitalization at Duke Hospital, a former nurse from the same institution died in Tennessee from a transfusion reaction of the same etiology. A description of a case of successful hemodialysis, where Kell antibodies had caused acute renal failure, was published a few days later.[6]

Management

The potential reversibility of the renal lesion of acute tubular necrosis and the possibility of a fatal outcome in case of persistence of the lesion or of mismanagement during the critical period place an enormous responsibility on the physician in charge of such a patient. Attempts at modifying the lesion directly, such as decapsulation, lumbar block, or adrenal steroid treatment, did not show convincing efficacy and have been abandoned. It became apparent that the tubular cells possess considerable ability to regenerate and regain function if the basement membrane remains intact. It is now generally recognized that the aim of therapy must be to have the patient survive the critical period until spontaneous recovery occurs.

Three principles of therapy are involved: first, to limit the development of biochemical changes as far as possible; second, to anticipate, prevent if possible, and treat, when dangerous, clinical complications directly or indirectly associated with the biochemical changes; and, third, to determine when conservative management threatens to be insufficient and artificial means of reversing potentially fatal biochemical changes should be utilized.

Although excellent discussions of the problems of acute renal failures exist,[7] it seems worthwhile to use the data of this case for a short recapitulation of the main points of conservative management of this condition. Because of the nature of the functional defect, the regulation of water and electrolyte balance and the excretion of the products of protein breakdown, are major points for consideration.

Overhydration is the most frequent error in the management of such patients. Throughout the period of oliguria in the hospital, this patient received only an average of 450 ml. of fluid per day, representing a positive water balance of frequently less than 300 ml. per day. This was formerly considered to be insufficient for replacing the insensible losses. However, it is now realized that endogenous sources supply water when protein, fat, or carbohydrate are oxidized and that this water replaces a portion of the insensible loss. In patients with excessive tissue destruction, the catabolism may be so great as to lead to detectable edema on fluid intakes of less than 500 ml. per day.

This patient showed no signs of dehydration. She lost 3.8 kg. (8.4 lb.) during the 12-day period of oliguria, an average of about 0.3 kg. per day. This weight loss results from inadequate caloric intake, which is usually unavoidable and harmless for this period of time. No weight loss in such patients indicates overhydration. Accurate daily weight measurements and physical examination are controls for the state of hydration.

Caloric intake is necessarily inadequate during the period of oliguria. Protein is contraindicated because of potassium and nitrogen. Fat is difficult to administer. The patient is frequently anorexic, nauseated, and vomiting and usually tolerates oral feedings poorly. The parenterally given fat emulsions presently available are not satisfactory. Then, too, most patients have adequate endogenous fat stores to tide them through the period of oliguria. Carbohydrate, therefore, is the main exogenous source of calories. As oral feedings are usually more hazardous and the fluid volume must be restricted, intravenous infusion of 30 to 50% dextrose, fructose, or invert sugar (a mixture of both) is desirable. Such concentrated solutions can be infused into the interior or superior vena cava for a matter of days without producing chemical phlebothrombosis. A polyethylene catheter is passed from the femoral or antecubital vein by a percutaneous technique. Cut-downs or other unnecessary surgery are contraindicated.

The importance of carbohydrates is not primarily to supply calories but to spare protein. Prevention of excessive breakdown of body protein is mandatory, but the protein-sparing effect of nonprotein calories is limited. It has been shown that in healthy fasting subjects 100 Gm. of dextrose per day achieved the maximum protein-sparing effect and prevented ketosis.[8] Considering the stress situation of the severely ill patient, 100 Gm. of dextrose may not be sufficient. Increase in intake of parenterally given carbohydrate must be limited, however, by consideration of the simultaneous increase in fluid intake. The patient discussed in this paper received 140 to 180 Gm. of sugar, representing an average total intake of 624 calories per day for the oliguric period, and did very well.

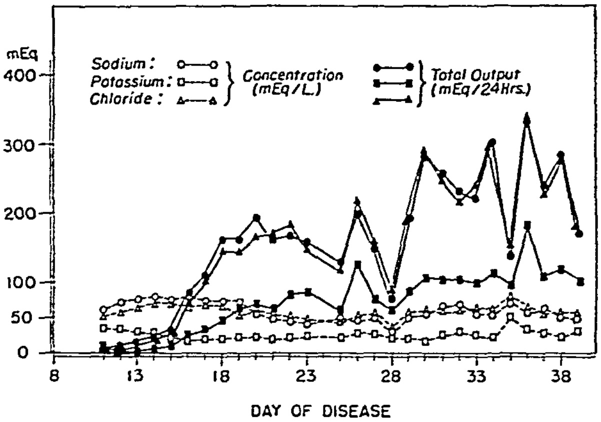

Fig. 3.—Urine electrolytes during oliguric and diuretic period of acute tubular necrosis.

Potassium intake is almost always contraindicated. Without any exogenous supply, potassium originating from endogenous processes, such as tissue breakdown and cation shifts, makes hyperkalemia the most important and most dangerous complication in acute renal failure. The electrocardiogram, not the serum value, is the best guide for determining the clinical danger of hyperkalemia. The patient showed the first electrocardiographic changes suggesting hyperkalemic effect on the eighth day of oliguria. Such minimal changes should be considered serious, and attempts to combat the toxic effects of potassium begun immediately. The usefulness of calcium and of insulin in hyperkalemia is well established.[9] The efficacy of testosterone or norethandrolone (Nilevar) has never been convincingly proved,[10] but it apparently does no harm if used for a few days; it is not used routinely in this clinic. Cation exchange resins in the form of the sodium salt are available on an experimental basis in most treatment centers for renal diseases. The results in this and other clinics are encouraging, but the resins must be used with caution as hypokalemia may develop. It must be realized that acidosis, hyponatremia, and hypocalcemia aggravate the toxic effects of potassium.

Disturbances of sodium balance, usually iatrogenic, and their management may become a very difficult problem in patients with acute renal failure. Chloride and phosphate are of less immediate concern. The serum phosphorus in this patient rose to a maximum of 14.6 mg. % on the 13th day of oliguria. The significance of phosphate retention lies mainly in its contribution to acidosis.

Acidosis was present in this patient, as was evident from serum carbon dioxide and blood pH. An attempt to correct the acidosis was not seriously considered in this case. The pH deviation was not excessive and the precipitating factor was not loss of sodium, but retention of acid metabolites. Under these circumstances, addition of alkaline salts is usually not useful and may be dangerous because it causes overloading of the intravascular compartment with water through osmotic effect. Extrarenal removal of acid metabolites would be the logical procedure, but it was not necessary in this case.

Antibiotics were administered as a precautionary measure, in addition to respiratory isolation. Antibiotics are not used routinely in this clinic, but respiratory isolation for the patient's protection is considered desirable. The use of a urethral catheter, indwelling or intermittent, should be avoided if possible because of the increased danger of infection.[11]

In this patient the diuretic phase did not offer any problems. The kidneys, of course, were "water-losing kidneys," being unable to concentrate. The nonprotein nitrogen level did not return to normal for two weeks after the diuresis began. This is the usual course. A much longer period of time is necessary for other kidney functions, as for instance phenolsulphonphthalein excretion, to return to normal.[12] Six to 12 months may be necessary for the maximum restoration of tubular function. No difficulties should be encountered in managing the electrolyte and water losses during the diuretic period. The main task is to be aware of them. Excessively massive diuresis indicates overhydration, which can be avoided.

Use of sedatives, analgesics, antibiotics, etc., should be omitted if possible, or the importance of the kidneys for handling the respective compound carefully evaluated. Use of digitalis should be avoided because of the antagonistic effect of potassium; if the serum potassium is reduced by artificial means, the patient may die of digitalis intoxication.

Acute tubular necrosis may be a benign disease. It is so, indeed, in the majority of cases, with proper management. The over-all mortality is assumed to be 20%. Uncomplicated cases of acute tubular necrosis should not be fatal. Problems arise in patients with complicating trauma, infection, labor, or surgery. Conservative management is usually adequate. There remain a number of instances, however, where biochemical changes are too rapid to be compatible with a two-week or more survival of the patient. It cannot always be predicted which patient belongs in this category. In such cases, the availability of an artificial kidney is of immeasurable value.

Summary and Conclusions

Acute tubular necrosis developed after an incompatible blood transfusion due to anti-Kell antibodies in the patient's serum. These antibodies were undoubtedly provoked by one of three previous transfusions. The incompatibility was detectable only by the indirect antiglobulin cross matching procedure.

This near fatal transfusion reaction reemphasizes the absolute necessity of employing the indirect Coombs cross matching procedure in addition to the saline or albumin method for every transfusion and particularly for those patients with a history of previous transfusions or pregnancy. The course of this patient's illness was benign, except for the duration of the period of profound oliguria, which was slightly longer than the average of 11 days. A benign clinical picture while oliguria still persists is no full guarantee for a benign outcome.

The chances for successfully managing acute tubular necrosis by conservative means are excellent in skilled hands. Because of the potential dangers to life which are present during the oliguric period even in the apparently benign case, it is highly desirable to have an artificial kidney available.

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OPACIFICATION OF RADIOLUCENT BILIARY CALCULI

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Biliary calculi are identified radiographically usually as defects in contrast medium-filled biliary structures, less frequently by the density of the calcium content, and occasionally by the presence of gas-containing fissures. Recently, an additional x-ray finding for biliary calculi has been described. Radiolucent biliary calculi were identified by their opacification after prolonged iopanoic acid (Telepaque) administration.[1] The observation of opacification of biliary calculi was made while exploring possible advantages of prolonged iopanoic acid administration in patients whose gallbladders failed to visualize or visualized faintly after the conventional examination with 3 Gm. of iopanoic acid. These patients were placed on a four-day regimen of 3 Gm. of iopanoic acid per day, 1 Gm. after each meal. A relatively fat-free diet was observed during this period. The x-ray examination was made on the morning of the fifth day, with the patient fasting. We have called this prolonged preparation for cholecystography "the four-day Telepaque test." Although an occasional patient complained of diarrhea during this interval, the test was well tolerated.

The opacified biliary stones were characterized radiographically by a generalized rather faint increase in the over-all density of the stones and a sharp increase in the linear density outlining the periphery of the stones. For this reason we have termed this opacification phenomenon "the rim sign" of biliary calculi. Opacification of stones in the gallbladder occurred both in the presence and absence of gallbladder visualization after the four-day iopanoic acid test. Opacification of common duct stones occurred in the absence of common duct visualization.

The incidence of opacifying calculi among all radiolucent biliary calculi could not be determined because the patients examined were a selected group. The opacification of the stones was observed in 3 of 34 patients examined by this method or a slight modification of it. The purpose of this article is to report a case in which the opacification of radiolucent biliary calculi occurred, and the reproduction of this phenomenon in vitro.

Report of a Case

A 79-year-old man was admitted to Denver General Hospital on Aug. 30, 1957, complaining of chills and fever. At a previous admission in 1954, he was found to have diabetes mellitus and adenocarcinoma of the prostate proved by transurethral resection; a bilateral orchiectomy was performed at that time.

On present examination the temperature was 37.5 C (100 F); rales were heard at the base of the right lung; diffuse abdominal tenderness was present; the testes were absent. Laboratory studies revealed a hematocrit of 33%; the white blood cell count was 35,600 per cubic centimeter, with 85% polymorphonuclear cells, 9% stab cells, 5% lymphocytes, and 1% monocytes. Urine was negative for sugar and acetone but loaded with pus and bacteria. Chest x-ray was within normal limits. The patient was given 2

From the Division of Radiology (Dr. Salzman) and the Division of Surgery (Drs. Watkins and Rundles), Denver General Hospital and the University of Colorado Medical Center.

units of blood, tetracycline (Achromycin), and supportive treatment, with improvement. On Sept. 13, the patient appeared jaundiced. The total bilirubin level was 7.4 mg. per 100 cc. The jaundice gradually subsided during the following week.

A plain x-ray of the abdomen on Sept. 16 failed to reveal any opaque biliary calculi (fig. 1*A*). A cholecystogram on Sept. 25, after the patient had been given 3 Gm. of iopanoic acid, showed only a faint visualization of the gallbladder (fig. 1*B*). A repeat cholecystogram after the patient had received 3 Gm. of iopanoic acid per day for four days revealed opacification of numerous large, irregularly shaped calculi in the distal right and left hepatic, common hepatic, and common bile ducts to the ampulla of Vater. The gallbladder was faintly visualized and major biliary ducts were not visualized (fig. 1*C*). On Oct. 16 a film of the abdomen showed that opacification of the radiolucent biliary calculi had disappeared. The gallbladder was still faintly visualized (fig. 1*D*). A repeat cholecystogram on Oct. 19, after another regimen of 3 Gm. of iopanoic acid per day for four days, revealed reopacification of the bile duct stones and faint visualization of the gallbladder (fig. 1*E*). A plain film of the abdomen taken Nov. 14 showed disappearance of the radiolucent bile duct stones and the gallbladder (fig. 1*F*).

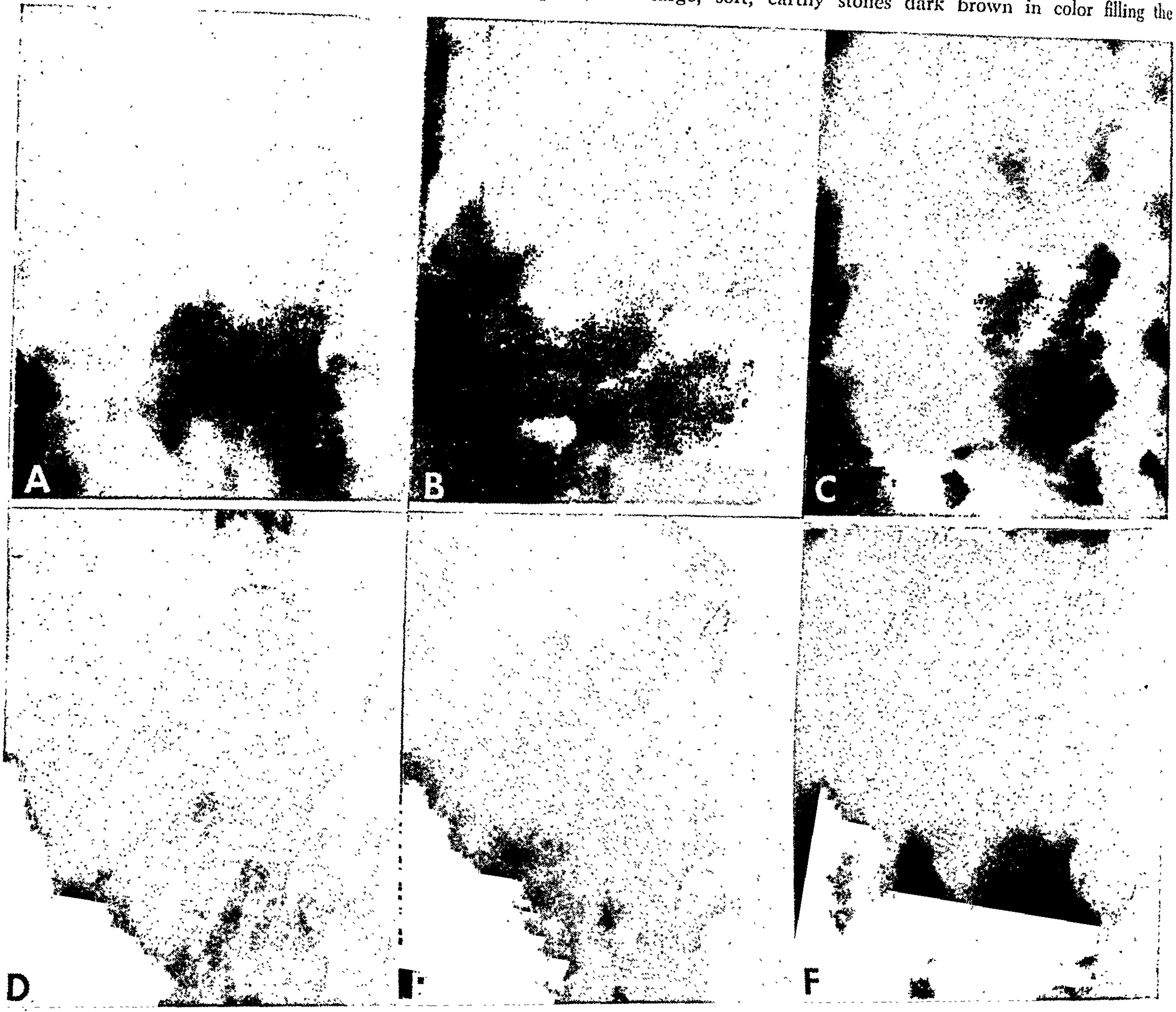

Fig. 1.—*A*, preliminary x-ray of abdomen showing no opaque biliary calculi. *B*, after 3 Gm. of iopanoic acid, faint visualization of gallbladder, residual iopanoic acid in colon. *C*, after four-day iopanoic acid test, large irregular stones fill distal right and left hepatic, common hepatic, and common bile ducts; faint visualization of gallbladder. *D*, two weeks after four-day test, disappearance of opacification of bile duct stones; gallbladder still faintly visualized. *E*, after repeat four-day test, bile duct stones opacified again; faint visualization of gallbladder. *F*, three weeks after repeat test, disappearance of opacification of bile duct stones and gallbladder.

On Oct. 26, a scrotal abscess appeared which was incised and found to communicate with the urethra. A cystostomy was done on Oct. 30. The patient's course was complicated by bronchopneumonia, and he died Nov. 28, 1957. The significant autopsy findings were bronchopneumonia, healed pyelonephritis, biliary cirrhosis, chronic cholecystitis, cholelithiasis, and choledocholithiasis. There were numerous large, soft, earthy stones dark brown in color filling the distal hepatic, common hepatic, and common bile ducts to the ampulla of Vater, as was seen on the clinical x-ray examinations. These bile duct stones were packed tightly in the region of the cystic duct and partially obstructing the cystic duct, which may explain the faint visualization of the gallbladder at cholecystography. The gallbladder contained thin yellow fluid and numerous stones of a different character from those found in the major bile ducts. The gallstones were small, oval, hard, and deeply pigmented.

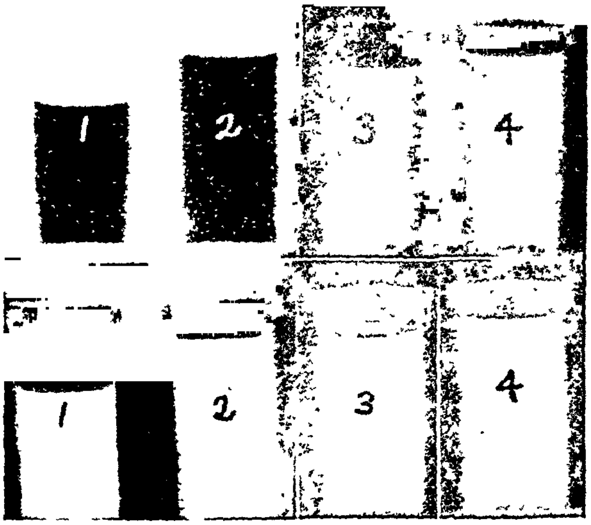

Fig. 2.—In vitro studies. *Top*, immediate x-ray. 1, gallstones in iopanoic acid bile. 2, common duct stones in iopanoic acid bile. 3, gallstones in normal bile. 4, bile duct stones in normal bile. *Bottom*, after three days at room temperature. Only bile duct stones in iopanoic acid bile show increased opacification.

In Vitro Studies

The opacification of the radiolucent bile duct stones and the failure of the radiolucent gallstones to opacify clinically were reproduced in vitro. Samples of gallstones and bile duct stones obtained at autopsy were immersed in plastic tubes of iopanoic acid bile and normal bile. The iopanoic acid bile was obtained at laparotomy from the gallbladder of a patient who had received 3 Gm. of iopanoic acid the evening prior to the operation. The normal bile was obtained at autopsy from a normal gallbladder. The tubes were x-rayed immediately (fig. 2, *top*), kept at room temperature, and x-rayed again four days later (fig. 2, *bottom*). The bile duct stones in the tube of iopanoic acid bile were strikingly opacified and there was no additional opacification of the bile duct stones in the normal bile or of the gallstones in the iopanoic acid bile and normal bile. This corresponded to the observations made on the clinical x-ray examinations of the patient. This evidence supports the idea that the opacification of radiolucent biliary calculi is the result of a deposition of iopanoic acid or an iodinated product of iopanoic acid on the surface of the stone. Furthermore, the failure of the gallstones to opacify and the opacification of the bile duct stones indicate the opacifying quality is inherent within the stone and not the result of instability of the colloidal system of the iopanoic acid bile. Work is in progress to determine the substance in some biliary calculi which is responsible for the opacifying quality.

Summary

The four-day iopanoic acid (Telepaque) test is a prolonged preparation for cholecystography for opacification of radiolucent biliary calculi. In vitro studies showed that opacification is a result of a deposition of iopanoic acid or an iodinated product on the surface of the stones. The opacifying quality is inherent in the stone and is not due to an instability of the colloidal system of the bile.

West Sixth Avenue and Cherokee Street (4) (Dr. Salzman).

The iopanoic acid used in this study was supplied as Telepaque by Winthrop-Stearns, Inc., New York.

References

1. Salzman, E., and Warden, M. R.: Telepaque Opacification of Radiolucent Biliary Calculi: "The Rim Sign," Radiology, to be published.

ANTIBIOTICS AFTER APPENDECTOMY.—We have also noted a serious complication from the use of antibiotics, namely postoperative pseudomembraneous enterocolitis. There has been increasing evidence in the past 18 months that some of the appendiceal deaths could be attributed to acute pseudomembranous enterocolitis occurring postoperatively. Most of the cases have occurred in middle aged or elderly individuals. Antibiotics, sometimes of the broad-spectrum type, were given following operation. During the postoperative period, usually between the sixth and tenth day, these patients experienced a rather sudden onset of crampy abdominal pain, abdominal distention, fever, chills and diarrhea. Within a short time they went into profound and unremitting shock in the terminal stage. The picture has been frequently confused with severe diffuse peritonitis or rupture of a hollow viscus. The passage of many watery, greenish stools has been a frequent, but by no means, invariable finding. Tremendous amounts of fluids are lost into the gastrointestinal tract and this probably accounts for the severe shock and dehydration. Micrococcus pyogenes may almost invariably be cultured in the diarrheic stool in the severe cases.—F. A. Bothe, M.D., Appendectomy, *The Surgical Clinics of North America*, December, 1957.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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MUMPS IMMUNIZATION

Edward B. Shaw, M.D.

MUMPS is a very rare infection during the first few months of life even when there is intimate exposure. The resistance of the infant is probably not due to transplacentally acquired antibodies, for, unlike the situation which obtains in measles, protective antibodies against mumps do not long persist in the serum of those who have had the disease. Gamma globulin prepared from plasma gathered from the population at large is completely without value against the risk of this infection. Only the gamma globulin prepared from plasma of those who have been hyperimmunized against mumps virus has any probable protective effect. This effect is at best unpredictable and not completely reliable.

There is no satisfactory method for protection against mumps after exposure. Susceptibility may be determined by means of the skin test with material prepared from the virus which is grown on embryonated eggs. The tuberculin reaction–like positive response is supposed to indicate the probability of previous infection and immunity. Negative tests are inconclusive, and the presence of egg protein may lead to false-positive results.

Some degree of passive immunity against mumps may be conferred by the use of hyperimmune gamma globulin, which is commercially available. It is impossible to evaluate adequately this protection. The communicability of mumps is relatively low; about one-third of the adult population is said to be immune because of previous undiagnosed and perhaps subclinical infection. Apparently successful protection may simply be the result of residual immunity in the subject or of insufficient exposure. Failures of protection are not infrequently encountered when susceptibility is accompanied with intimate exposure.

Active immunity against mumps may be induced by two injections of the commercially available vaccine which has been cultured on embryonated eggs. This immunity cannot be induced in the interval between exposure and the appearance of disease, so that it does not provide the greatest potential usefulness for a method of active immunization. Such active immunization, although it does not appear quickly enough to protect from known exposure, is of such short duration that it cannot be of great value to the susceptible adult who may be exposed to the disease from time to time unless immunization is repeated at least annually. Unfortunately, many adults react somewhat violently to the injections of the vaccine.

Children who are exposed to mumps should be allowed to develop the disease—but obviously very little can be done to prevent this should one choose to do so. There is much less likelihood of infection after mumps exposure than is the case with measles or chickenpox. Probably the low order of communicability accounts for the fact that so many adults escape the disease during childhood only to develop it in later years. Orchitis and oophoritis rarely develop before puberty, and the other complications of mumps which may occur in childhood, including meningitis, are not usually of great severity.

Deliberate exposure to the disease in childhood is another matter. This may be desirable for the child as the only means of inducing lifelong immunity, but it introduces the potential risk of secondarily exposing adults who may then have the illness with greater severity and sometimes with permanent sequelae. It is desirable that the child acquire this infection before puberty as the best source of permanent immunity and the prevention of the disease during adult years, at which time serious complications are more frequently encountered. The exact protective effect of methods of artificially induced active or passive immunization are difficult to evaluate and are certainly not completely reliable.

Clinical Professor of Pediatrics, University of California School of Medicine, and Chief, Communicable Disease Department, Children's Hospital, San Francisco.

ORGANIZATION SECTION

PUBLIC RELATIONS INSTITUTE IN CHICAGO—AUGUST 27-28

The A. M. A.'s 1958 PR Institute at the Drake Hotel in Chicago, Aug. 27-28, billed as the "V. I. P. Meeting," is designed for physicians, medical society staff personnel, and others working in the medical public relations field. The workshop-styled program will get down to PR practicalities at its opening session with a discussion of medicine in a changing world. From the lead-off "What Do You Know?" session, the meeting will move into deliberations on "What Have You Got To Say?" "How Do You Say It?" "Who Do You Know?" and "Are They Listening?" Top people in related fields, including communications and human relations, will take part in the program.

REPORT PUBLISHED ON HILL-BURTON PROGRAM

The results of a two-year study of the Hill-Burton Hospital Survey and Construction Program will be available in booklet form Aug. 1, from the Committee on Medical and Related Facilities of the A. M. A. Council on Medical Service. Sections in the report include introduction, summary, conclusions, recommendations, federal grants-in-aid, background and basic administration, general hospitals, tuberculosis hospitals, public health centers, mental, chronic disease, and nursing home facilities, diagnostic or treatment centers, rehabilitation facilities, and other reference material. In addition to reviewing the legislative background of the act and much other data, reports are included on field surveys made in Arkansas, California, Connecticut, Georgia, Illinois, Iowa, Kentucky, Maryland, Michigan, Mississippi, Montana, New Jersey, Oregon, and Washington. A limited number of copies will be available to individual physicians and medical societies.

NEW FILM ON FOOD QUACKERY

How "medicine men" dupe the public into spending millions of dollars on unnecessary or overpriced nutritional products is shown in a new American Medical Association film. Prepared for airing over local television stations under the auspices of local medical societies, this 27-minute film, "The Medicine Man," dramatically pinpoints the fight against quackery in the food and nutrition field.

The film singles out problems which stem from health lecturers who travel from town to town giving misinformation on nutrition as a tie-in to plugging their products of questionable merit and from door-to-door salesmen who misrepresent the value of nutritional products. The film also shows how the medical profession cooperates with the Food and Drug Administration and voluntary agencies such as the National Better Business Bureau in the crackdown on these food quacks.

First showing of the film will be at the A. M. A. Public Relations Institute, Aug. 27-28, at the Drake Hotel, Chicago. Prints will be available to local medical societies after Sept. 15 from the A. M. A. television film library.

RENEWAL OF ILLINOIS LICENSES

Most physicians living outside of Illinois and holding an Illinois license to practice may not be aware that all licenses expired automatically on June 30 under a new law which went into effect on July 1.

The last legislature passed a law requiring re-registration by July 1 in every even numbered year beginning with 1958. Because the Department of Registration and Education had only the addresses in effect at the time the original licenses were issued, and not subsequent changes, it has been able to notify only a small percentage of licensees, both in and out of the state.

Physicians desiring to renew their licenses in Illinois should write to the Department of Registration and Education, Capitol Building, Springfield, Ill., giving name, address, and license number and sending $6, the biennial re-registration fee. The biennial re-registration measure had the backing of the Illinois State Medical Society because it will provide a current published list of those entitled to practice medicine and make a check possible on those operating unlawfully.

WORK ABSENCE GUIDE TO BE PUBLISHED

The A. M. A. Committee on Medical Care for Industrial Workers (a joint committee of the Councils on Medical Service and Industrial Health) is currently working on a "Guide for Measuring Work Absence Due to Illness and Injury." To obtain additional data for such a booklet, the Committee will publish a "preliminary guide" which will be used in field surveys and will be mailed on about Aug. 1 to companies, individuals interested in the subject, and medical societies. Medical societies may send information on their activities in this area to the Committee.

COUNCIL ON NATIONAL DEFENSE

The following two papers were presented at the Sixth National Medical Civil Defense Conference in San Francisco on June 21, 1958. This annual conference is sponsored by the A. M. A. Council on National Defense.

The Hon. Leo A. Hoegh was appointed by President Eisenhower on June 24 as the director of the new Office of Defense and Civilian Mobilization. Prior to that, he served as administrator of the Federal Civil Defense Administration for 11 months.

The Hon. R. Walter Riehlman, of Syracuse, N. Y., is the second ranking minority member of the House Committee on Government Operations and a member of its military operations subcommittee which conducted extensive hearings on civil defense for national survival in 1956. As a result of these hearings, a number of important recommendations were made to strengthen and improve the national civil defense program.

The role and leadership of the federal government to civil defense determines, to a large measure, the activities of state and local governments. These two papers are being published as a matter of interest to the medical profession because they outline the current thinking and efforts of the executive and legislative branches of the federal government in the field of civil defense.

FRANK W. BARTON, *Secretary.*

CURRENT CONCEPTS OF THE FCDA

Leo A. Hoegh, B.A., J.D., Washington, D. C.

I know of no group that is more receptive to civil defense, no group that is more responsive to our planning, and no group with more significance to the ultimate survival of this nation, than the members of the American Medical Association. We appreciate your splendid cooperation and performance.

Medical Care

We proposed, some time ago, that the responsibility for health and medical care of the surviving population be delegated to the Public Health Service of the Department of Health, Education, and Welfare. We want to delegate this whole responsibility to the PHS, and, along with it, the responsibility for writing the medical portion of the National Civil Defense Plan which we have drawn and which I will discuss more fully later.

At no time did we consider doing this without first bringing it before the A. M. A. The latest opportunity for full discussion came in a meeting, late in April, of the Civil Defense Committee, the chairman of which is Dr. Lueth. This was a fine meeting. Dr. Lueth himself called it a "most worthwhile and productive type of conference." I know it was most helpful to me. Dr. Blasingame, General Manager of the A. M. A., wrote to me to say:

> It is my pleasure to advise you that by action of the Board of Trustees at a meeting on May 30, 1958, the Association concurs in the principle of the proposed delegation—provided that it is specified that the states, local political subdivisions thereof, and other organizations and agencies concerned with the health of the population surviving an enemy attack on the United States will be afforded an opportunity to participate actively in and otherwise contribute to the planning, preparation, and implementation of the contemplated nationwide health and medical care program designed to utilize *nonfederal facilities and resources.*

Of course we would not want it any other way, and both the Public Health Service and FCDA have so assured the Civil Defense Committee and, as a consequence, the A. M. A. itself. As soon as possible after July 1, formal negotiations will be opened with the Secretary of Health, Education, and Welfare, concerning this proposed new delegation.

It is essential that all physicians and all medical facilities be counted as part of this nation's civil defense because when you look squarely at it, civil defense to be effective will involve every human being, professional or nonprofessional, and every facility that can be found. How we go about this is, of course, the real subject of the contract FCDA made with the A. M. A. nearly a year ago. Under this contract, the A. M. A. will study, develop, and recommend the planning, training, and operational organization needed as a basis for a national emergency care plan for treatment and care of casualties and noncasualties prior to, during, and after an attack.

The A. M. A. Commission on National Emergency Medical Care is directing this study—using the Minneapolis-St. Paul area as an example—so that the A. M. A. can come up with recommendations covering (1) the use of professional and nonprofessional personnel of the medical and related

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Administrator, Federal Civil Defense Administration.

Read before the Sixth Annual National Medical Civil Defense Conference, San Francisco, June 21, 1958.

professions preattack and immediately postattack; (2) the functions and responsibilities of the medical profession that may be delegated and performed by paramedical personnel; (3) the training and education that is needed by all health personnel, professional and nonprofessional, for wartime operational capability, and the sorting of casualties.

We expect quite a bit, don't we, for our $150,000? This, however, is only a part of our expenditures that should interest you. You will be glad to know that we are back in the MEND program—Medical Education for National Defense. We are going to put $135,000 next year, on equal shares with the Army, Navy, and Air Force, in this program to acquaint instructors with medical problems anticipated in time of national disaster so that graduates are better prepared to assume the responsibilities of military or civil emergency medicine.

Radiologic Defense

Now, in this concept of keeping civil defense functions within those areas best equipped to deal with them, there are certain "holes" that we feel it is our responsibility to plug. There is, for instance, no normal civil agency equipped or trained to deal with the problem of radiation monitoring. Therefore, we have instituted our own program for radiologic defense. It should be of special interest to you because it is critical to the survival of the maximum number of people.

There literally is no place in the whole United States that can consider itself immune to radioactive fall-out caused by nuclear weapons. Every individual must know where there is invisible danger and where there is comparative safety. This can be determined only if we build true radiation monitoring capability throughout the entire country. We are building it. We have undertaken a program that has two parallel actions: We are multiplying our training course—at national headquarters and in the regions—and we are concentrating on science teachers who in turn can teach many others how to use the variety of instruments necessary for scientific measurement.

Simultaneously, we are delivering sets of radiologic instruments and instructor kits to the high schools of the nation. Six thousand schools will have the instruments in time for school opening in September, and another 9,000 will get them in time for the second semester. This will equip half of the high schools in this school year, and by June, 1959, over one million students will be properly trained. All high schools will be furnished the equipment and instructor manuals by 1960.

We are furnishing radiologic devices to the states and target cities. Through their civil defense personnel, it is expected that over 100,000 city and state employees in police, fire, and other departments will be properly trained during the next year. The federal network of fixed monitor stations will use the facilities of all federal agencies. Instruments are being distributed to 221 Weather Bureau stations and to 600 Civil Aeronautics Administration stations. Also included are 79 Air Weather Service monitoring points under the Department of Defense. By the end of 1958, the federal network will have available about 900 monitoring points over the nation, operating on a round-the-clock basis.

We feel certain that through these actions we will build the monitoring capability that we must have. It is possible that fall-out resulting from an attack on this country could claim twice as many lives as blast and heat.

Shelter Policy

But knowing where intense radiation exists is of little value if we are not prepared to protect ourselves against it. This is one of the reasons for the recent announcement of a national shelter policy which will give us for the first time a logical and workable approach to this phase of civil defense. Under this policy, the administration will undertake the following five courses of action:

1. Inform every American of the possible effects of nuclear attack and of the actions he and state and local governments can take to minimize them. Every American must know the hazard and how to meet it.
2. Make sampling surveys of existing structures, particularly in larger cities, to determine shelter capabilities. Many facilities already afford some fall-out protection. We must get this information.
3. Accelerate research to show how shelter may best be incorporated in both existing and new structures and to improve shelter designs.
4. Construct a limited number of prototype shelters for varied geographical and climatic areas. They will have practical peacetime uses, such as underground parking garages, school and hospital cafeterias, subways, highway fills, and homes.
5. Incorporate fall-out shelters in appropriate new federal buildings that will be constructed from now on. Federal example is an indispensable stimulation to state and local government and private investment for the same protective construction.

In essence what we have here is a do-it-yourself shelter program with strong federal leadership, guidance, and example. Through this we can simultaneously accomplish three things: 1. We can create protection at compartively low cost. 2. We can help to insure that all fall-out shelter is so arranged that the areas have a daily common use while remaining available for emergency. 3. We can avoid the tremendous tax burden that would be laid on the nation if a massive federally financed shelter construction program were undertaken.

Incidentally, as individuals and home owners, you might like to know that FCDA currently is distributing a new, plain-language, illustrated publication showing how to create fall-out shelter in a dwelling at comparatively low cost.

National Plan

The fact that every person in the United States could be affected by fall-out is the best reason I know why everyone, without exception, must consider himself a part of civil defense. Civil defense, I am sure you know, is no special force or magic device. Properly, it is a combination of all nonmilitary actions that can be taken to protect our nation and our people.

These actions cannot be at random or without direction. They must be planned in advance and executed according to predetermined patterns. Hence we have completed the National Civil Defense Plan after many months of intensive work by many people and with the guidance and assistance of many groups and organizations. The plan has been coordinated with federal government agencies and with state and local governments as well. You have made a valuable contribution in its preparation.

It sets forth the specific mission of each level of government and, for that matter, of the individual citizen. In this one document are all of the basic civil defense principles and responsibilities for protecting life and property. It creates a civil defense channel of coordination down which instructions will be transmitted and up which requests for assistance will be made. It states our mission clearly—"To protect life and property from the effects of attack by preparing for and by carrying out emergency functions to prevent, minimize, and repair injury and damage." It then sets forth the functions and, step by step, how the mission is to be accomplished, and by whom.

Detailed explanations for special services have been or will be drafted as annexes to the plan. One of these annexes—the Medical and Health Plan—will become the obligation of the Public Health Service by delegation to the Department of Health, Education, and Welfare.

This National Plan can become fully effective only if the Senate approves a House-passed measure, the Durham Bill (H. R. 7576), which is now in one of its committees. The plan is keyed to the principle that the federal government has the responsibility for the over-all direction and coordination of civil defense action—something only hinted at under existing law.

Civil defense must be taken seriously today by every level of government and by every citizen. Certainly civil defense is taken with utmost seriousness in Russia, according to dispatches from Russia just last week. The United Press said that every Soviet citizen is being required, this year, to take a 22-hour training course, with a wider and more detailed study program to follow.

The newspaper *Soviet Patriot* revealed th DOSAAF—the Voluntary Society for Assistance the Army, Air Force, and Navy—has set itself th prime task of instructing the entire population antiaircraft, antiatomic, antichemical, and an bacteriological defense. It also said that within th next two years, civil defense units will be esta lished in every factory, collective farm, scho university, and other institutions throughout Ru sia. Looks like they are copying our plans. Th are doing by compulsion what we hope accomplish through persuasion and guidance, b our way is the best way. When the American pe ple are told of the threat and how to meet it, a when they have leadership by government, th will respond.

We do not anticipate or expect war. We simp recognize that as long as city-destroying weapo exist, we must prepare against them. The enem in desperation or sheer idiocy, could push t wrong button. Therefore, we will continue to add the very substantial progress we already have ma in federal guidance and federal actions. I am thin ing now of certain functions which only go ernment can perform—such things as warnin communications and control, survival plannin and recovery, all backed up by research a education.

I will not go into the technicalities of all of the here, because I want to devote my remaining ti to the all-important question of control. I do th particularly because in the Civil Defense Co mittee meeting of which I spoke earlier, the seemed to be some concern about martial law an military assumption of civil defense responsibilitie The questions arose out of a misunderstood milita address to our state civil defense directors.

There is no question today of the military's rol in relation to civilians. Very quickly it is this: Th military is to be prepared to support the civ efforts if its mission permits. In other words, th primary role would be military; but if they are a position to do so, then they have to be prepare to support the civil effort. We do not expect th the military will ever take over.

We are doing everything possible to strengthe government's capacity to operate in an emergenc through our Continuity of Government Program We say that it is necessary to retain this loca government. So our primary objective is to see tha the civil government is so strengthened that n "martial law" will become necessary.

Control is critical to survival. Government at all levels must be able to continue operating and directing in any emergency. Four elements are necessary to insure this: First, lines of succession for key government personnel must be established. second, alternate sites for conducting government must be chosen, fully equipped, and kept in full operating condition. Third, there must be duplication and safe storage of those records essential to continued government operation and for the protection of individual rights. Fourth, provision must be made for the full use of all government resources—personnel, facilities, and equipment.

Plans are well under way for discharging these control and communications responsibilities at the federal level. Some states and cities also are moving in concert, but of course much more needs to be done, as it does in all areas of our responsibilities. At the same time, we must reach every individual with the guidance that may mean the difference between living and dying. This is one of our greatest challenges, but one we must not fail to meet, because despite everything I have said here, civil defense first, and most importantly, is acutely personal. Individuals might have to depend upon their own knowledge and resourcefulness for days or weeks after a major attack. There are five simple steps to safety—that everyone must know: (1) warning signals and what they mean, (2) your community plan for emergency action, (3) protection from radioactive fall-out, (4) first aid and home emergency preparedness, and (5) use of Conelrad—640 or 1,240 for official directions.

I realize that many of our citizens expect a civil defense to be built somewhere and shipped out to them, complete, and functioning. There are even more, perhaps, who would be willing to buy civil defense, just as they buy military defense with their tax dollars. They miss the point that since nuclear war would affect everyone, there would be no one to employ. Civil defense is everyone's business.

No, we can't buy civil defense, we must live it. There is no other way. All we can do is to make people understand this, see to it that the hardware is in place, and give the people the leadership and the know-how they must have in time of crisis. When governments are prepared and capable of leading, I am convinced the people will rally to their support—only then will we have effective civil defense. This is a challenge to all of us but especially to government. We will—we must—meet it.

THE CONGRESSIONAL PROGRAM FOR CIVIL DEFENSE

R. Walter Riehlman, Washington, D. C.

Very briefly, I shall summarize recent congressional action affecting civil defense and outline in general terms the civil defense legislation now pending in Congress, together with a few comments on what I consider the essential elements of a workable civil defense program for our nation.

First, however, I should like to congratulate the American Medical Association, and particularly the Council on National Defense, for its fine work in civil defense. The continuing support of the Association, as well as the support of the medical profession in general, has contributed significantly to the civil defense work of our subcommittee on military operations, and I am sure its support has been of immeasurable help to the Federal Civil Defense Administration.

Your presence at this conference today evidences the personal interest of you gentlemen of the medical profession, and I commend you for that interest. No single group in our society can perform a greater civil defense service than can the medical profession.

In time of emergency, your skills and energy will be essential to the saving of many lives. Virtually the entire recovery effort will center around and be dependent on the vital task of the medical profession.

Almost equally important is the civil defense service which can be performed by the medical profession before an enemy strikes. As leaders in your local communities, you gentlemen significantly influence public opinion. People respect your judgment and tend to follow the example you set, particularly with respect to civic and community affairs. Your attitudes toward civil defense and other public affairs mean a great deal in crystallizing public opinion. Your personal interest in and concern with civil defense will have much to do with the general attitude the public takes toward this very important subject.

In this connection, permit me to give a special word of praise for one of your distinguished colleagues and a close friend of mine, Dr. Fred Hiss, of Syracuse, N. Y. In addition to being the protector of my good health, Dr. Fred Hiss is actually my mentor in the ways of civil defense. On my visits to him he may forget to tell me how much I owe, but never does he forget to preach civil defense. And gentlemen, he knows the ins and outs of it, believe me. My visits may stretch out way beyond the appointed time, but the knowledge I gain is invaluable. An outstanding physician and a wonderful person to know, this gentleman is fully aware of his responsibilities as a civic and community leader and represents the best traditions of the medical profession in every respect.

I should also like to pay my respects to Federal Civil Defense Administrator Leo Hoegh. Last month the House military operations subcommittee.

U. S. Congressman, 35th Congressional District, Syracuse, N. Y., second ranking minority member of House Committee on Government Operations and member of its Military Operations Subcommittee.

Read before the Sixth Annual National Medical Civil Defense Conference, *San Francisco, June 21, 1958.*

of which I am the ranking minority member and former chairman, had the privilege of interrogating Governor Hoegh regarding civil defense policies and programs of the federal government. His sincerity of purpose was most impressive, and I believe I can say on behalf of the subcommittee that the determination with which he has undertaken his task as FCDA administrator is encouraging to us all.

As some of you may know, our subcommittee on military operations has done a great deal of work in the field of civil defense. I am aware that sometimes we have been referred to as the chief critics of the FCDA, but I prefer to consider our relationship with the FCDA as more of a partnership arrangement. I am sure Governor Hoegh agrees with me in this respect, and I want to thank him personally for his many kind remarks about the work of our subcommittee.

The most recent civil defense work of our subcommittee was in connection with President Eisenhower's reorganization plan no. 1 of 1958, which was transmitted to Congress on April 24th of this year. Under the provisions of this plan, the Federal Civil Defense Administration and the Office of Defense Mobilization will be merged to form a new agency called the Office of Defense and Civilian Mobilization. The new agency will be located in the Executive Office of the President.

This reorganization represents a significant development in civil defense at the federal level. In my view, it deals with one of the three principal requirements of civil defense at the federal level today. Briefly summarized, these requirements are (1) a federal organization which has the prestige and status required to deal effectively with other federal agencies and with state and local governments and which is capable of planning and executing a realistic national program for civil defense; (2) federal authority to provide financial assistance to the states and localities for certain administrative and personal expenses; and (3) a federal program to assist the states in developing protective measures against nuclear weapons effects.

Federal Organization

Before speaking of the second and third requirements, let us consider for a moment this very important matter of federal organization. The question of how best to organize for civil defense has been a matter of study in the federal government for more than a decade. The President's plan did not spring forth in full bloom. Rather, it was the culmination of long study and planning extending back to the end of World War II.

Until 1949, responsibility for civil defense planning was carried out by the War Department and the Department of Defense, whose main concern in the matter was to identify the types of programs needed to preserve the industrial mobilization base in the event of a future war. In 1949, civil defense planning responsibilities were vested in the National Security Resources Board, which had been created by the National Security Act of 1947. It was concerned with a wide range of nonmilitary defense matters, including economic stabilization, resource allocation, and defense production. This board, the NSRB, developed a general plan for civil defense, and in late 1950—after the beginning of hostilities in Korea—two actions were taken to establish a functioning civil defense program.

Almost simultaneously, a Federal Civil Defense Administration was established by executive order, and legislation providing for a statutory agency of the same name was submitted to Congress. That legislation became the Federal Civil Defense Act of 1950, sometimes called Public Law 920 of the 81st Congress.

This emergency legislation provided the framework for an operating civil defense program, but experience has demonstrated that the task assigned to the operating agency—the FCDA—was too limited in scope. In effect, major nonmilitary defense planning was left as a function of the NSRB, while the FCDA was given the task of establishing the operating program of civil defense. The remaining functions of the NSRB later were vested in the Office of Defense Mobilization, which has operated as a part of the President's Executive Office.

This division of nonmilitary defense functions between ODM and FCDA has continued until the present time. It has been the cause of much confusion and no doubt has hindered the development of an effective program. The President's plan will go a long way toward eliminating this source of confusion. For the first time, we will have a single source of policy guidance at the highest level of the federal government. In my opinion, this is one of the most important developments in civil defense since World War II.

For years we have been trying to establish a workable framework for civil defense in the federal government. And this transition to the new Office of Defense and Civilian Mobilization is the latest step in a long and arduous effort to move out of the planning stage and into a functioning program. This has been a prime objective of the military operations subcommittee from the inception of our civil defense studies. Nearly four years ago, while chairman of the subcommittee, I prepared a concurrent resolution which would permit the transfer of FCDA to the Department of Defense. The FCDA would thereby become a fourth department coequal with the three military departments.

My purpose was to break the log-jam then besetting the civil defense program. I was convinced of the need to move out of the planning stage and into an operating civil defense program. And the close relationship between civil defense and active military defense indicated to me that civil defense should be virtually an adjunct of our military program. That measure, which was introduced the next year as H. Con. Res. 108, sought to avoid the many side-issues and confusing relationships existing in civil defense by placing unmistakable authority in an operating agency with great prestige and with basically similar duties.

This resolution, together with other measures introduced in the House, was the basis of the comprehensive and exhaustive civil defense investigation undertaken by the subcommittee under the chairmanship of Congressman Chet Holifield of the state of California. Subsequently, at the conclusion of our investigation, I introduced a new bill (H. R. 2239) designed to revamp our entire civil defense effort and place the program in a separate Cabinet-level Department of Civil Defense. The bill also would authorize basic new civil defense functions, including the construction of shelters and vastly increased federal assistance to state and local civil defense programs.

One other essential feature of the bill is that the civil defense functions of the ODM would be transferred to the new Department of Civil Defense. In this respect, of course, my bill and the President's reorganization plan are in basic agreement. In either case, complete responsibility for federal civil defense policy would be vested in a single agency of high standing in the federal government.

Now, the President's plan will accomplish this organizational objective, but it does not change the basic authority underlying the federal civil defense program. Reorganization plans are by nature limited to organizational changes. New functions can be added only through new legislation.

Federal Assistance for State and Local Programs

This brings us to the second and third requirements. In addition to improved organization, the federal civil defense effort must include substantially increased support for state and local civil defense programs. I am aware of the current debate over whether the federal government is performing too many functions which might better be performed by the states. Without going into the issues of that debate, I can only say this: The states and localities have not been able to develop the level of civil defense preparedness required; and, whether we like it or not, such preparedness can be achieved only if the federal government assumes a major role both in terms of leadership and in financing.

I am convinced that the FCDA should be authorized to provide financial assistance to states and localities for civil defense personnel and administrative expenses and should be authorized to assist in developing positive protection against nuclear weapons effects, including shelter protection against blast and radioactive fall-out. The bill which I introduced (H. R. 2239) would authorize both of these functions within the framework of a comprehensive national master plan for civil defense. Legislation sponsored by the FCDA would also authorize a part of these functions but only on a much more limited scale.

The FCDA-sponsored legislation (H. R. 7576) passed the House unanimously and is now pending before the Armed Services Committee of the Senate. This bill would authorize federal contributions for state and local civil defense personnel and administrative expenses, and it would authorize the FCDA to donate and maintain radiologic detection instruments.

These are two very important functions, and both are badly needed. But they will not, by themselves, do the total job required in civil defense today. One of the major additional requirements is a federal shelter construction program. Because of the nature of modern weapons, shelter construction, together with radiologic detection equipment, is a vital factor in assuring the survival of our population.

Protective Measures Against Nuclear Weapons

One of the first things we need to do is to get radiologic detection devices into the hands of a large number of people throughout the United States. These people should be thoroughly trained in the use of such devices. Today, only a small percentage of our population has any conception of how to use radiologic monitoring and detection equipment. The nature of the threat requires that we have possibly 100 million such devices in use. Virtually the entire population should participate.

Once we develop this type of capability, once we are able to measure and monitor redioactive fall-out, then we can make maximum use of existing structures to shield ourselves from the deadly effects of fall-out. Simultaneously, we should begin the construction of shelters specifically designed for fall-out protection and a reasonable degree of blast protection. Obviously, we cannot expect to do this job overnight, but we should get started without further delay.

At the recent hearings of our subcommittee on military operations, the technical experts of FCDA advised us that enough test data have been developed to enable us to start constructing civil defense shelters immediately. Naturally, further improvements and refinements in shelter designs and construction techniques will be forthcoming, but we cannot wait for absolute perfection. Such improvements can be incorporated as we go. The important matter is that we have the required technical data, and we know the job that needs to be done.

Governor Hoegh has mentioned (see this issue, page 1748) the national shelter policy which he announced at our recent hearings. This national shelter policy represents an important step toward more effective civil defense in the United States. While some of us may disagree as to the specific measures required and how we should go about obtaining the shelter protection we need, there is no debate over the basic requirement itself.

It is my understanding that, under the new national policy, a survey of existing structures will be made to obtain definite information on the capabilities of these structures to provide fall-out shelter. Even now, certain buildings, mines, subways, and tunnels afford some fall-out protection. Designs of shelters will be perfected to assure the most economical and effective types. A number of prototype shelters suitable to different geographical and Climatic areas will be constructed and tested by actual occupancy for realistic periods of time.

Several key personnel of the Naval Radiological Defense Laboratory remained in a shelter at the Nevada Proving Ground during an actual test shot this past year. To my mind, this is ample proof of their confidence in the shelter designs that have been developed. The prototype structures to be built under the new shelter policy may be in underground parking garages, schools, hospitals, industrial plants, and residences and apartments. And, of course, it should be observed that these facilities will also have practical peacetime uses.

I share the opinion of most members of Congress that in programs like this the government should lead the way and set a good example. Therefore, it is gratifying to know that, hereafter, plans for future government buildings, be they large or small, will contain facilities for shelter.

H. R. 7576, the bill now pending in the Senate, does not deal with the shelter program, but it will have a bearing on the success of the new shelter policy as well as on any other shelter policy that might be adopted in the future. In view of the closely related requirement for a substantial radiologic monitoring and detection capability, the authority contained in H. R. 7576 is extremely important.

If the FCDA can proceed to purchase and distribute to the states radiologic monitoring equipment, we can begin to build the type of monitoring program required. In the future, such a program could be expanded so that eventually the entire population might develop a monitoring and detection capability.

Support for FCDA Program

One additional matter I wish to discuss with you this morning is the problem that FCDA has had in obtaining congressional support for its program. This problem is directly reflected in congressional action on FCDA appropriations requests. Since its beginning in 1951, FCDA has asked for a total of 2 billion dollars to set up and operate its vast program. Only about 450 million dollars has been appropriated by Congress for this entire period. In other words, FCDA has been forced to struggle along with less than 25% of the money it believed necessary to successfully launch and operate this very important program. This 450 million dollars spent for civil defense during the past eight years amounts to approximately 1% of the 40 billion dollars spent each year on our military defense.

I have no quarrel with the spending of this money for military defense. I am wholeheartedly in favor of a strong military program. My objection is that so little has been appropriated for the other phase of our defense effort, the civil defense phase. Now, I do think the situation is beginning to improve. This year FCDA was granted substantially the amount of funds it requested, and there are signs that the future will see even greater improvement.

In the past, one of the roadblocks in the way of full congressional support for civil defense was the lack of a realistic over-all National Civil Defense Plan. I must confess that we in Congress have at times been critical of the seeming laxity of FCDA in not presenting to us something definite to indicate just where we are headed in civil defense. Actually, this problem is closely tied in with the requirement for improved organization at the federal level.

If the impending reorganization results in the development of a realistic and comprehensive program, then I'm sure the Congress will be willing to increase its support for the agency and the program. I think it is basically as simpe as that. Congress has not been inclined to support civil defense in the absence of a realistic national program. Once we achieve a civil defense organization with the status and capacity required to develop such a program and once such a program is presented to Congress, then I think we will see a different attitude on the part of Congress.

This is not to imply that the present agency has not sincerely attempted to do the job, and I do not wish to leave that impression. In my opinion, they simply have not had the authority, the status, and the tools that they need. I recognize that there is no single answer to the complex and changing problems of civil defense. I have endeavored to indicate my own views, with particular reference to pending legislation, including the President's reorganization plan.

Summary and Conclusions

In summary, the reorganization plan holds promise of much improved nonmilitary defense organization at the federal level, with the elimination of confusion and duplication in policy direction. H. R. 7576 will, to a limited extent, increase the federal role in support of state and local civil defense programs. And the recently announced National Shelter Policy constitutes a recognition of the fundamental shelter requirement in civil defense. Taken together, these measures represent a substantial step in the right direction, although they fall short of the total program I have supported in proposed legislation. Despite my own misgivings, however, I sincerely believe that we ought to do everything we can to support this start toward a more realistic civil defense program.

There are many other aspects of civil defense deserving attention at this time, but I shall mention only one more. That is the extremely important matter of health and medical considerations under the new federal organization. Throughout our entire civil defense study and investigation the subcommittee's effort to achieve a stronger federal program has been staunchly supported by the American Medical Association. The Association has endorsed my bill (H. R. 2239), and it has followed every development with great interest. In connection with our consideration of the President's reorganization plan, the Association submitted a lucid statement pointing up the importance of the medical and health aspects of civil defense. I should like to include the following excerpt from that statement:

> The basic concept of national mobilization is accepted as the "will of the people to resist." This concept depends on the sustained physical and mental health of the people and as such has interested the American Medical Association for many years.
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> In its concern with the health and medical aspects of civil defense, the Association has recognized, for a number of years, the urgent need for federal leadership, direction, and coordination. The Association believes that civil defense, like military defense, is an integral part of national defense which requires greater federal responsibility and leadership.
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> More specifically, the Association is concerned with the status, in any federal agency, of the office responsible for medical and health activities. The Association is convinced that medical and health activities are one of the most, if not the most, important function in sustaining the "will of the people to resist."

I can only echo these sentiments and say that our subcommittee is also concerned with the status of health and medical activities in the new Office of Defense and Civilian Mobilization. We know of the vital importance of these activities in any civil defense program. I wish to commend the Association for this strong statement in support of our civil defense work, and I assure you that our subcommittee will continue its efforts to secure a realistic civil defense program for our country.

COUNCIL ON MEDICAL SERVICE

STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 5

EARLY NEONATAL MORTALITY STUDY IN DELAWARE

The Committee on Maternal and Infant Mortality was established in 1937 by the Delaware State Medical Society at the request of the Delaware State Board of Health. It was composed of one member from each county of the state and was directed to work with the state board of health "in an effort to abolish as soon as feasible the present system of midwifery in Delaware."

With the cooperation of the state board of health, the committee began a study of maternal deaths in 1937. The questionnaire method was used, and each death was classified as to cause and preventability. A review of infant deaths was included in the committee's work in 1943. At this time the infant death cases were not reviewed individually but only to the extent that information was available from the health department.

Beginning in 1955, the infant deaths studied have been limited to those occurring in the hebdomadal period (the first seven days after birth). Data are obtained on each individual case by reviewing the hospital charts and in some cases by interviewing the physicians concerned. This work is done by members of the committee or by other physicians at the committee's request.

The membership of the committee has increased to eight and now includes four pediatricians, two general practitioners, and two obstetricians, with one of the obstetricians serving as chairman. The two previous chairmen served seven and three years. Members are retained on the committee if willing to serve; geographical representation is adhered to by the president in his appointment of new members.

Scope of Study

The purpose of this study is to account for deaths which occur during the first seven days of life. Objective analyses of the various phases of obstetric and pediatric management of these cases is expected to reveal the preventable factors, if any, in these deaths and thereby to lead to a lowering of the neonatal mortality rate. The committee

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This is the fifth and last of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States.

Committee members are: W. L. Crawford, M.D., Chairman, Rockford, Ill., R. B. Chrisman Jr., M.D., Coral Gables, Fla., Philip S. Barba, M.D., Philadelphia, Harold S. Morgan, M.D., Lincoln, Neb., Garland D. Murphy, M.D., El Dorado, Ark., Howard A. Nelson, M.D., Greenwood, Miss., J. L. Reichert, M.D., Chicago, Donald A. Dukelow, M.D., Consultant, Chicago, Philip F. Williams, M.D., Consultant, Bala Cynwyd, Pa., Edwin J. Holman, Consultant, Chicago, and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

also studies the maternal deaths that occur in Delaware, but as these are becoming very few (three in 1956), this phase of the program is incidental to the main study. (The committee is striving to reduce this number to zero, however.)

Method of Operation

Case-Finding.—During the early part of each year the state board of health furnishes to the committee the identifying information on each maternal death and each hebdomadal infant death which occurred in Delaware during the previous year. The information supplied includes the name and address, the date of death, the cause as indicated on the death certificate, and the name of the hospital.

Collection and Processing of Data.—The chairman and members of the committee and other physicians designated by the committee in the various hospitals of the state review the hospital charts and other records to determine race, period of gestation, age at death, autopsy results, cause of death, contributing factors in the infant, and contributing maternal factors. These physicians evaluate each case as objectively as possible and classify it as preventable, possibly preventable, or nonpreventable. Each preventable and possibly preventable case is further classified as previable premature (500-999 Gm.), viable premature (1,000-2,500 Gm.), or full-term (more than 2,500 Gm.). (Since some "previable" infants live, deaths of fetuses in this weight range are classified as possibly preventable whenever preventable factors are discovered.) A brief summary is made for each of these cases, including the cause of death and the preventable factors.

Follow-up and Use of Findings.—Statistics are compiled indicating the total number of live births, the number of hebdomadal deaths, the hebdomadal death rate, the number of deaths in the first 24 hours and the rate of such deaths per 1,000 live births, and the proportion of premature (previable and viable) and full-term infants in each of these classifications. An annual report in the *Delaware State Medical Journal* lists these statistics, as well as the causes of death, for each of the 10 Delaware hospitals giving maternity care. The report also provides summary data on each death considered preventable or possibly preventable and discusses other important aspects of these cases.

The need for more and better autopsies is emphasized in these reports. It is pointed out that the exact cause of death can be determined only by composite analysis of the baby's and mother's clinical courses, by laboratory studies, and by postmortem examination of the baby. The percentage of cases for which the cause of death remained undetermined was almost inversely proportional to each hospital's autopsy percentage. It is pointed out that such categories as prematurity and atelectasis should not be given as the primary causes of death, since autopsy usually reveals a more specific cause. Correctible conditions are discussed frankly, and each report contains recommendations for improvement of the study.

No direct follow-up of individual preventable factors has been made, as anonymity in the study is considered essential.

Results

During 1943, the first year that infant deaths were considered in the committee's review, the rate was 43.3 per 1,000 live births. By 1956 it had been reduced to 21.9. In the 15 year period from 1940 to 1955 the early neonatal death rate dropped from 23.9 to 14.4. In 1955 the rate ranged from 10.6 to 22.2 among the individual hospitals. Although the numbers of live births in these hospitals are too small to give statistical significance to one year's figures (the range was from 159 to 2,831), it is believed that the steady decrease in the rates in several of the hospitals over a period of years indicates a great deal of improvement in care. The autopsy rate was 45.8% for all hospitals, with the largest hospital having a rate of 74.4%.

Of the 10,569 live births in 1955, 152 resulted in death within the first seven days of life. Four of these deaths occurred at home, and of the hospital deaths, 51 (34.3%) were classified as previable premature, 61 (41.3%) as viable premature, and 36 (24.3%) as full-term.

Of the 152 early neonatal deaths, 15 (9.8%) had preventable factors. This percentage is not large, but it does indicate the need for continued studies of this type to discover what deficiencies still may be present in the care of these newborn infants. Four of the 15 (one viable premature and three full-term) were classified as preventable and 11 (two previable, seven viable premature, and two full-term) as possibly preventable.

Comments and Conclusions

The members of the Committee on Maternal and Infant Mortality have studied early neonatal deaths occurring in Delaware in some detail for the past two years. They believe that improvements can be made, but they feel that there has been much progress even though the study has been conducted more or less informally. They do recommend, however, that each hospital set up a committee, including representatives from the departments of pediatrics, obstetrics, anesthesiology, and pathology, and that these committees study each neonatal death within a month after it occurs. The committee believes that a more accurate statistical analysis could be made at the end of each year if some more frequent and uniform method of receiving and reviewing cases could be established.

MEDICAL NEWS

FLORIDA

State Medical Election.—The Florida Medical Association has installed the following officers: Dr. Jere W. Annis, Lakeland, president; Dr. Ralph W. Jack, Miami, president-elect; Dr. Samuel C. Harvard, Brooksville, first vice-president; Dr. Walter E. Murphree, Gainesville, second vice-president (reelected); Dr. Joseph W. Douglas, Pensacola, third vice-president; Dr. Samuel M. Day Jr., Jacksonville, secretary-treasurer (reelected); and Dr. Shaler A. Richardson, Jacksonville, editor (reelected).

Miami Researchers Win Award.—Dr. Robert J. Boucek, associate professor of cardiology, University of Miami School of Medicine, Coral Gables, has received the major award of 300 pounds sterling in the Ciba international competition for studies related to aging. His paper, honored among 62 projects submitted by research workers in 19 different countries, was on "The Effect of Tissue Age and Sex upon the Metabolism of Rat Collagen." Dr. Boucek's co-workers were Nancy L. Noble, Ph.D., J. Frederick Woessner Jr., Ph.D., Kung-Ying Tang Kao, Ph.D., and Harry R. Elden, Ph.D. The research was financed by the Howard Hughes Medical Institute. Other awards in this competition were given to research workers in Tanganyika, London, Minneapolis, Los Angeles, Prague, Geissen (Germany), Bern, and Maebashi City (Japan).

ILLINOIS

Chicago

Dr. Huggins Honored.—The Charles Mickle fellowship for the year 1958 has been awarded by the University of Toronto to Dr. Charles B. Huggins, director, Ben May Laboratory for Cancer Research, University of Chicago, for his "contributions in the field of cancer." The award is made to that member of the medical profession and related sciences who is considered by the Council of the Faculty of Medicine of the University of Toronto "to have done most during the preceding 10 years to advance sound knowledge of a practical kind in medical art or science." The fellowship is accompanied by an award of $1,000.

Society News.—The Chicago Society of Industrial Medicine and Surgery has elected the following officers: Drs. Walter J. Phillips, president; George J. Cooper, vice-president; Bille B. Jennan, secretary; and Charles M. Drueck, treasurer.——The Chicago Ophthalmological Society has elected the following officers: Dr. J. Vernal Cassady (South Bend, Ind.), president; Dr. Clifford P. Sullivan, president-elect; Dr. Manuel L. Stillerman, vice-president; Dr. Joseph S. Haas, secretary-treasurer; Dr. Theodore N. Zekman, councilor; and Dr. David E. Shoch, recording secretary.——The following officers have been elected to the Chicago Orthopaedic Society for 1958-1959: president, Dr. Carlo S. Scuderi; vice-president, Dr. John H. Moe; president-elect, Dr. Newton C. Mead (Evanston); secretary, Dr. William A. Larmon; and treasurer, Dr. Charles V. Heck.

Dr. Clark Appointed Chairman of Department of Surgery.—Dr. Dwight E. Clark has been appointed chairman of the department of surgery of the University of Chicago, effective July 1, succeeding Dr. Lester R. Dragstedt, who becomes emeritus next year, but resigned from the chairmanship to complete research he is conducting. Dr. Clark was an intern, resident, and instructor in the University Clinics of the the University of Chicago, 1937-44, when he became chief of surgery and commanding officer of the Army Medical Corps's Oak Ridge, Tenn., hospital. He returned to the university in 1947 as associate professor of surgery and in 1951 was appointed professor and senior attending surgeon of Billings Hospital, and secretary of the department. Dr. Clark is vice-president of the Society of Nuclear Medicine and a member of the board of governors of the American College of Surgeons.

Pavilion for Infant and Maternal Research.—Dedication of a new research laboratory, a one-million-dollar remodeling of the former Mother's Aid Pavilion and now named the Mother's Aid Research Pavilion of the Lying-In Hospital of the University of Chicago Clinics, was held June 13. Two of the three floors have a series of laboratories including equipment for radioactive materials: the third floor will be used for steroid hormone studies; the second floor has laboratories for investigations in pathology, cytology, microbiology, and biochemistry. Facilities for parent education classes, exercise rooms, and elements important in obstetrical practice are on the second floor. One of the hospital's outpatient clinics and various offices are on the first floor. Appointments to the Lying-In staff for the

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

research program include Dr. Kimball C. Atwood, of the Oak Ridge Laboratories, who becomes associate professor of medical genetics, effective Sept. 1. The research program in cytology is under Dr. George L. Wied. Research into causes of infant deaths is under Dr. Edith L. Potter. A scientific program was held June 14 which included as speakers Dr. Duncan E. Reid, Boston; Dr. George W. Corner, New York City; Dr. Nicholson J. Eastman, Baltimore; and Donald H. Barron, Ph.D., New Haven, Conn.

Mother's Aid Research Pavilion, Lying-In Hospital, University of Chicago Clinics.

LOUISIANA

Study of Tropical Diseases.—The Louisiana State University School of Medicine, New Orleans, has sent eight teachers from American and Canadian medical schools to Latin America for training in tropical diseases. Following two days of orientation in New Orleans, the teachers proceeded to the tropics for eight weeks of observation of diseases and health programs. Five went to Costa Rica, Panama, El Salvador, and Guatemala; the other three went to Puerto Rico, the Dominican Republic, and Haiti. The program is made possible by the voluntary cooperation of medical and public health leaders in the respective countries, the Overseas Missions of the U. S. State Department, and the Pan American Sanitary Bureau of the World Health Organization. This is the last group to receive such fellowships under a grant of $120,000 to the university from the China Medical Board of New York, the primary interest of which is medical education in the Far East and in the U. S. The program has been in operation for three years, during which time 69 fellowships have been awarded to teachers from 53 medical schools. Louisiana State University has received approval of a grant from the National Institute of Allergy and Infectious Diseases to continue this program for five more years on a broadened basis to include teachers and graduate students from nonmedical institutions.

MICHIGAN

Skin Bank to Aid Treatment of Burns.—A living "skin bank" has been established in the surgery department of the University of Michigan Medical Center, Ann Arbor. Reserved for the treatment of serious burns, the bank contains narrow strips of human skin 12-thousandths of an inch thick. These are stored in a nutrient fluid at controlled temperatures to provide "homografts" in emergencies. The homograft used at the Medical Center is taken from the donor's back, just below the shoulders. Dr. Irving Feller, instructor in surgery, has charge of the skin bank. The homografts in the skin bank are being obtained, with the permission of relatives, from persons who have just died.

Tuberculosis in Michigan.—The Michigan Tuberculosis Association has reported that chest x-ray surveys of the Michigan Department of Health in 1957 were nearly twice as effective as in previous years in finding suspected cases of tuberculosis A total of 8,059 tuberculous suspects were found among the 399,364 films taken. This was a rate of 20.2 suspects for every 1,000 x-rays. In the preceding five years, the rate ranged from 10 to 12. An increasing portion of the newly reported tuberculosis cases are being found through selective x-ray surveys. A total of 5,011 cases of tuberculosis were reported last year in Michigan. This is a reduction of 9% from 1956. In recent years new cases of tuberculosis have fluctuated between 5,000 and 6,000, showing an over-all gradual decline. In the first four months of 1958, there were 491 more new cases reported than during the first four months of 1957.

Personal.—Dr. Harry E. Carnes, a member of the clinical investigation staff, Parke, Davis & Company, has been appointed director of medical correspondence and editor of *Therapeutic Notes*, published monthly in five languages for physicians throughout the world. Dr. Carnes will assist as consultant in the medical education and training of the sales staff, and assist the hospital medical service staff. ——Dr. Gordon B. Myers, chairman, department of medicine, Wayne State University College of Medicine, Detroit, has been appointed head of the new university service in internal medicine at Harper Hospital. With the addition of Harper Hospital, Wayne now directs three services in internal medicine, the others at Receiving Hospital.——Dr. Elwood A. Sharp, of Grosse Pointe, medical assistant to the president of Parke, Davis & Company, has been elected an affiliate of the Royal Society of Medicine.——Dr. John R. McDonald, head of a section of surgical pathology in the Mayo Clinic and professor of pathology in the Mayo Foundation, Graduate School, University of Minnesota, Rochester, became director of pathology at the Harper Hospital in Detroit, July 1.

MINNESOTA

Clinic Lectures.—Dr. Geoffrey Watkinson, of the University of Leeds, England, gave a lecture on "Secretory Studies in Uncomplicated Peptic Ulcer, Hematemesis and Achlorhydria by the Use of 24-Hour Gastric Analysis" at the Mayo Clinic, Rochester, May 12. On May 14 he lectured on "Steroid Therapy in Ulcerative Colitis."——Dr. Nanna C. Svartz, head of the King Gustav V Research Institute and professor of medicine in the Caroline Institute in Stockholm, Sweden, spoke on "Isolation of the Rheumatoid Factor" at the Mayo Clinic, Rochester, May 21.

NEW YORK

Fellowships for Research at Rochester.—The University of Rochester has established a program of postdoctoral fellowships to be awarded graduates of approved medical schools to enable them to pursue research in the School of Medicine and Dentistry. The Buswell fellowships are made possible by the bequest of the late Mr. Ralph Hochstetter and are intended to assist "well qualified" doctors of medicine to prepare adequately for academic careers. Buswell Junior Fellowships will be awarded to medical graduates who have completed at least one year of internship or equivalent training. Research experience is not required. Junior fellows are expected to spend about 90% of their time in research or in advanced study in preparation for research. Fellowships will provide a basic stipend of $4,500 to $6,000 per year, and may be renewed with increments for a second or third year; $350 per year may be provided for each dependent. Buswell Senior Fellowships will be awarded to medical graduates who have held a Buswell Junior Fellowship for two or three years or have had comparable experience. Senior fellowships will provide a basic stipend of $5,500 to $8,000 per year, with provision for annual increments; $350 per year may be provided for each dependent. Applications will be received at any time. Information may be obtained from Dr. Lawrence E. Young, Chairman, Committee on Buswell Fellowships, University of Rochester Medical Center, 260 Crittenden Blvd., Rochester 20. N. Y.

New York City

Rappleye Scholarship Fund.—After 27 years as dean, Columbia University College of Physicians and Surgeons, Dr. Willard C. Rappleye has retired, and the alumni and teaching staff have decided to mark this occasion by setting up a special scholarship fund in his name. This will be a capital fund, the income of which will be used each year to assist needy students. Contributions may be sent to the Committee for the Willard Cole Rappleye Scholarship Fund, Room 3-424, 630 W. 168th St., New York 32.

Appoint Director of Department of Medicine.—Dr. Kenneth R. Crispell has been appointed professor and director of the department of medicine at New York Medical College, Flower and Fifth Avenue Hospitals. Dr. Crispell comes to New York from the University of Virginia Medical Center, Charlottesville, where he was associate professor of internal medicine. He will succeed Dr. Linn J. Boyd, who resigned from this post after 30 years to become director of the expanded division of graduate studies. Dr. Crispell was a fellow in internal medicine at the Ochsner Clinic in New Orleans, and a fellow in biophysics at Tulane University. He went to the University of Virginia as a Commonwealth Fellow in 1949. He became assistant professor in internal medicine in 1951, and associate professor in 1955.

PENNSYLVANIA

Philadelphia

Dr. Grice Comes to Philadelphia from Harvard.—Dr. David S. Grice, assistant clinical professor of orthopedic surgery, Harvard University, Boston, has been appointed chairman of the University of Pennsylvania School of Medicine's department of orthopedic surgery, effective Sept. 1. Dr. Grice will succeed Dr. Paul C. Colonna, who will retire following 16 years as chairman of that department.

Medical History Lectures.—Dr. George Rosen, Columbia University Faculty of Medicine, will give the first annual Victor Robinson Lecture in History of Medicine at Temple University School of Medicine Sept. 23, 4 p. m., in the medical school auditorium, on "Victor Robinson—A Romantic Medical Historian." This lectureship is named in honor of Dr. Robinson, professor of history of medicine at Temple University from 1929 until his death in 1947.

Society News.—The Philadelphia Academy of Surgery has elected the following officers: Adolph A. Walkling, president; W. Emory Burnett and J. Montgomery Deaver, vice-presidents; William T. Fitts, secretary; Stephen D. Weeder, treasurer; and Jonathan E. Rhoads, chairman, Committee on Scientific Business.——The following officers of the Philadelphia Roentgen Ray Society have been elected for the year 1958-1959: president, Dr. Herman W. Ostrum; vice-president, Dr. John T. Brackin Jr. (Abington); secretary, Dr. Roderick L. Tondreau; treasurer, Dr. Randal A. Boyer; and counselor-at-large, Dr. Harold J. Isard.

Woman's College Plans Research Wing.—The Woman's Medical College of Pennsylvania has announced plans for a new 2-million-dollar wing to be constructed starting next fall at the northeast end of the present college building. Principally designed for research, the wing will consist of six stories and a basement. In the over-all plans, some diagnostic and treatment facilities are also included. A grant of $500,000 from the U. S. Public Health Service has been given to the college for laboratories, which with a matching amount already secured, will provide the research floor. The college is still soliciting funds to complete its 2-million-dollar goal needed to include the teaching and diagnostic facilities. The addition of the new wing with the expanded department of physiological chemistry reportedly will enable the college to take 20% more freshman students a year.

Personal.—Dr. Theodore H. Ingalls, formerly associate professor of epidemiology, Harvard University School of Public Health, Boston, joined the University of Pennsylvania School of Medicine faculty July 1 as professor of preventive medicine and epidemiology and will direct a Kellogg Foundation research project aimed at evaluation of periodic health examinations for the early detection and prevention of chronic diseases. He will also be responsible for directing a graduate research and training program in the university's department of public health and preventive medicine, headed by Dr. John P. Hubbard.——Dr. Lincoln Godfrey Jr., of the University of Pennsylvania Medical School, has been appointed director for research of the National Council on Alcoholism Medical Research Committee. As director, Dr. Godfrey will make a survey of research in the basic sciences preparatory to developing specific programs in alcoholism research.——Dr. Donald M. Pillsbury, chairman, University of Pennsylvania School of Medicine's department of dermatology, has been named president of the 12th International Congress of Dermatology, to be held in Washington, D. C., in 1962.

WASHINGTON

Fishing Derby in Idaho.—Scenic Priest Lake in Northern Idaho will be the site of the Doctors' Fishing Derby to be held Sept. 15 as an event of the 1958 convention of the Washington State Medical Association, according to Dr. O. Charles Olson of Spokane, derby chairman. The fishing derby will be headquartered at Linger Lodge at Priest Lake. Round-trip bus transportation will be provided from the Davenport Hotel in Spokane, where the convention will be held Sept. 14-17. Boats and out-of-state licenses will be provided to participants in the derby, and breakfast, luncheon, and an evening banquet will be served.

Personal.—Dr. Charles A. Evans, professor of microbiology, University of Washington School of Medicine, Seattle, has been appointed a member of the National Advisory Cancer Council of the U. S. Public Health Service.——Dr. Robert F. Rushmer, professor of physiology and biophysics, University of Washington, Seattle, gave "Cinefluorographic Studies of Cardiac Function" as the third W. Edward Chamberlain Lectureship, presented by the department of radiology in cooperation with the department of physiology, Temple University School of Medicine, Philadelphia.——Dr. Henry S. Bennett, professor of anatomy, University of Washington School of Medicine, Seattle, has been appointed to the National Advisory Health Council to the U. S. Public Health Service.

WYOMING

State Medical Election.—The newly elected officers of The Wyoming State Medical Society are: president, Dr. Luther H. Wilmoth, Lander; president-elect, Dr. Benjamin Gitlitz, Thermopolis; vice-president, Dr. Francis A. Barrett Jr., Cheyenne; secretary, Dr. Silvio J. Giovale, Cheyenne; treasurer, Dr. Carleton D. Anton, Sheridan; delegate to A. M. A., Dr. Albert T. Sudman, Green River; alternate delegate to A. M. A., Dr. Bernard J. Sullivan, Laramie; and executive secretary, Mr. Arthur R. Abbey, Cheyenne.

GENERAL

Surgical Conference in Nassau.—The first Bahamas Surgical Conference will be held at the British Colonial Hotel in Nassau, Bahamas, Dec. 29-Jan. 17. Speakers will include the following:

Drs. Richard H. Barrett, Hanover, N. H.; Lowell F. Bushnell, Los Angeles; John M. Chamberlain, Carl T. Javert, Gerald H. Pratt, and Charles S. Rogers, New York City; Bertha N. Davis-Clark, Randolph L. Clark Jr., and William O. Russell, Houston, Texas; Lawrence S. Fallis and Walter H. Seegers, Ph.D., Detroit; Lewis K. Ferguson, Arthur Finkelstein, Robert P. Glover, Louis E. Silcox, and Henry J. Tumen, Philadelphia; James H. Ferguson, and Donald W. Smith, Miami; and Raymond H. Rigdon, Galveston, Texas.

Special rates are available by writing directly to the manager of the hotel. For information write Dr. B. L. Frank, 23 E. 79th St., New York 21.

Railway Surgeons Meet in Seattle.—The annual meeting of the Western Association of Railway Surgeons will be held Aug. 7-9 in Seattle and will open with the presidential address by Dr. Bernard E. McConville, of Seattle. The annual Dr. William T. Cummins Memorial Lecture, "The Surgery of Peptic Ulcer," will be presented by Dr. Edward B. Speir, Seattle. Other participants will include the following: Drs. William A. McMahon, Matthew H. Evoy, Carl E. Chism, James D. Layman Jr., William J. Kelly, John R. Mullins, Stephen J. Wood, James F. Nelson, Carl J. Pinard Jr., J. Irving Tuell, and Dean K. Crystal, Seattle; William T. Duggan, San Francisco; and Roger W. Barnes, Los Angeles. A program of entertainment has been arranged, and the banquet will be held the evening of Aug. 8. For information write Dr. Graham J. Owens, Secretary, Western Association of Railway Surgeons, 906 Grand Ave., Kansas City 6, Mo.

Fellowships for Research and Clinical Medicine.—Deadlines for applications to the National Foundation for Infantile Paralysis, 301 E. 42nd St., New York 17, for postdoctoral fellowships in research and academic medicine or in the clinical fields of rehabilitation, orthopedics, and preventive medicine are Sept. 1 and Dec. 1. Financial support of the fellow varies according to his previous education, experience, marital status, and number of dependents. Compensation to the institution is arranged according to the program undertaken. For a full academic program, tuition and fees are allowed; for other programs, a sum not to exceed $1,250 per year (includes tuition) is provided. Awards are made on recommendation of the appropriate National Foundation Fellowship Committee. U. S. citizenship is required, but those who have filed a petition for naturalization will be considered. Partial fellowships are available for qualified veterans to supplement G. I. educational benefits.

Cardiac Conference in Denver.—The seventh annual Western Cardiac Conference, sponsored by the Colorado Heart Association, the Colorado State Department of Public Welfare, Fitzsimons Army Hospital, the University of Colorado School of Medicine, and the Veterans Administration Hospital, will be held Aug. 11-15 at the Phipps Auditorium, Denver. Guest speakers include Drs. Morgan Berthrong, Colorado Springs; Edwin Boyle Jr., Charleston, S. C.; William Dock, Brooklyn; Lt. Col. Laurence M. Hursch, M. C., U. S. Army, Denver; John W. Kirklin, Rochester, Minn., Edward Massie, St. Louis; Henry J. L. Marriott, Baltimore; John H. Moyer, Philadelphia; and George E. Wakerlin, New York City. Conference topics include "Modern Concepts of Electrocardiographic Interpretation" (Aug. 11-12), "Seminar on Hypertension" (Aug. 13), and "Recent Advances in Cardiovascular Diseases" (Aug. 14-15). A clinical pathologic conference and exhibits are planned. At the annual dinner Aug. 14, Dr. Dock will present "The History of Coronary Artery Disease." For information write the Colorado Heart Association, 1636 Logan St., Denver 3.

Meeting of National Medical Association in Milwaukee.—The 63rd convention of the National Medical Association will be held Aug. 11-14 at the Hotel Schroeder, Milwaukee. Guest speakers will include Judge Scovel Richardson, Washington, D. C.; Dr. Raymond D. Puritt, Rochester, Minn.; and Dr. Holland T. Jackson, Fort Worth, Texas. Panel discussions at the section meetings will include the following topics and moderators:

The Acute Abdomen, Dr. James M. Whittico, Jr., St. Louis.
Treatment of the Common Dermatologic Conditions, Dr. Carter L. Marshall, New Haven, Conn.
Office Gynecology, Dr. Robert C. Stepto, Chicago.
New Horizons in Ophthalmology and Otolaryngology, Dr. Gerhard D. Straus, Milwaukee.
A Planned Approach to Doctor Distribution in Urban and Rural Areas, Dr. Hiram L. Bell, New York City.

The president's address will be given by Dr. Arthur M. Townsend Jr. A symposium on "Gastric Ulcer" will be presented at the surgical section with Dr. William H. Sinkler Jr., as moderator. The Charles R. Drew Memorial Forum of Fundamental Science, moderated by Dr. Ellsworth E. Hasbrouck, Chicago, will be held the morning of Aug. 14, with a clinical pathological conference, "Stump the Audience," to be held that afternoon. Scientific and technical exhibits and a ladies' program are planned. Entertainment includes the president's ball August 14. For information write the National Medical Association, Inc., 1108 Church St., Norfolk 10, Va.

Foreign Seminar Tour.—A medical exchange team of American physicians conducted a series of seminars on immunopathology with doctors in Paris, France; Cologne, Bonn, Heidelberg, Freiburg, and Berlin, Germany; Basle, Seelisburg, and Zurich, Switzerland; and Prague, Czechoslovakia, June 8-July 5, under the sponsorship of the Unitarian Service Committee, a nonsectarian voluntary social welfare agency with headquarters in Boston. Field expenses of the team are supported by a grant from the Miles-Ames Foundation of Indiana. Object of the mission is the exchange of research information, to aid the advance of knowledge in the science of immunopathology in all countries whose representatives participate in the several symposiums, including the United States. Chairman of the exchange team was Dr. Lewis Thomas, chairman, department of pathology, New York University College of Medicine, New York City. Other members were: Dr. Chandler A. Stetson Jr., New York City; Dr. Frank J. Dixon Jr., Pittsburgh; Dr. Baruj Benacerraf, New York City; Dr. Robert A. Good, Minneapolis; and Dr. Ernest Witebsky, Buffalo, N. Y. Dr. Witebsky received special honors at Heidelberg University, from whose faculty he was expelled by the Nazis before World War II. The Unitarian Service Committee was established in 1940 to help refugees escape from Nazi Europe, but over the years it has adapted its program to changing needs in the fields of social work, education, medical exchange teams, community development, and rehabilitation carried on in Nigeria, Cambodia, Greece, Italy, France, and Germany.

San Francisco Golf Tournament Winners.—The recent annual tournament of the American Medical Golfing Association held on Olympic Club's two golf courses at Lakeside in San Francisco, was the largest attended in the 42-year history of the organization. The number of medical golfers who played was 374, and 350 of them stayed for the banquet in the evening, when more than $5,000 in prizes was distributed. There were 112 new members that participated in the tournament this year.

Dr. William O'Neal, of Pasadena, a surgeon, played even par 72 to win top honors. Dr. O'Neal has twice won the California State championship medal. Drs. Paul E. Travis, of Bell, Calif., and Frank Whittaker, of San Jose, Calif., both had gross scores of 73. The low net division was won by Dr. Gordon Erickson, of Encino, Calif. (62-12–64) and Dr. Fred Rice, of Indianapolis was second (94-28–66). Dr. Bob Reuter, of Fresno, Calif., made a hole in one on the fifth hole of the Ocean course.

Dr. Frank Whittaker, of San Jose, Calif., congratulates Dr. William O'Neal (holding trophy), of Pasadena, Calif. Dr. O'Neal stroked a par 72 to edge Dr. Paul Travis (second from left) and Dr. Whittaker (second from right) by one stroke. The low net division was topped by Dr. Gordon Erickson, of Encino, Calif. (far right), who finished two strokes ahead of Dr. Fred Rice, of Indianapolis (far left).

The winners of the eight flights were, in order: Drs. J. Dee Lansing, Arlington, Calif. (77-8–69); Winston Williams, El Segundo, Calif. (77-9–68); F. M. Binkley, San Francisco (79-12–67); J. H. Abramson, Sherman Oaks, Calif. (83-13–70); Ed Baker, Oakland, Calif. (84-15–69); John Growdon, Kansas City, Mo. (69); R. W. Burnett, Bakersfield, Calif. (68); and Robert Steeler, San Francisco (69).

The following officers were elected for the ensuing year: Dr. James McLaughlin, 1443 Cayugo St., Philadelphia, president; Dr. John Growdon, Kansas City, Mo., president-elect; Dr. Vincent deP. Larkin, Forest Hills, Long Island, N. Y., first vice-president; and Dr. William R. Smart, San Rafael, Calif., second vice-president.

The next tournament will be held at the Sea View Country Club, Atlantic City, N. J., June 8, 1959. Correspondence concerning membership should be addressed to Dr. McLaughlin at the above address.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 5, 1958		July 6, 1957
	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	1	1
Rhode Island	..	..	..
Connecticut	1	1	..
Middle Atlantic States			
New York	2	3	4
New Jersey	..	1	..
Pennsylvania	..	1	..
East North Central States			
Ohio	..	..	2
Indiana	..	1	2
Illinois	..	..	3
Michigan	..	1	6
Wisconsin	2	2	4
West North Central States			
Minnesota	..	..	..
Iowa	..	..	2
Missouri	..	1	3
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	1	2
Kansas	..	..	1
South Atlantic States			
Delaware	..	..	1
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	2	2	2
West Virginia	2	2	..
North Carolina	..	1	6
South Carolina	..	..	5
Georgia	1	1	3
Florida	1	8	..
East South Central States			
Kentucky	1	1	..
Tennessee	1	2	11
Alabama	1	1	1
Mississippi	..	5	2
West South Central States			
Arkansas	1	1	3
Louisiana	3	4	12
Oklahoma	..	3	5
Texas	8	12	45
Mountain States			
Montana	1	3	..
Idaho	..	..	1
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	1	1	1
Arizona	..	..	..
Utah	..	..	2
Nevada	..	..	1
Pacific States			
Washington	..	..	..
Oregon	1	1	1
California	1	2	13
Territories and Possessions			
Alaska	..	..	..
Hawaii	4	4	..
Puerto Rico	..	..	1
Total	34	67	147

FOREIGN

International Congress of Balneology.—The Czechoslovak Society of Physiotherapy is holding an International Congress of Balneology in Marienbad Sept. 8-13. One day will be devoted to choledocholithiasis, with an excursion to Karlovy Vary, Carlsbad. Papers will be read by scientists from Bulgaria, France, the German Democratic Republic, the German Federal Republic, Hungary, Poland, the Soviet Union, Sweden, and Czechoslovakia. The official languages of the Congress are English, French, Russian, German, Czech, and Slovak, and there will be simultaneous interpretation. Excursions and social events and a special program for family members of participants are planned. Inquiries should be addressed to the Secretary of the International Congress of Balneology, Řeznická 5, Prague 2, Czechoslovakia.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

American Board of Dermatology: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 20, 1958. *Oral.* Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), January 1959. Final date for filing application was July 1, 1958. *Oral Examinations* 1958 (Part II): Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports was July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Preventive Medicine: *Examination in Public Health.* St. Louis, Oct. 24-26. Final date for filing application is Aug. 15. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination.* Washington, D. C., Dec. 8. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application is Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Philadelphia, Sept. 15-16; Rochester, Minn., Oct. 20-21; Nashville, Tenn., Nov. 17-18; New York City, Dec. 15-16; Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: Various centers throughout the United States. *Written.* Sept. 12. Final date for filing application was July 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Avenue, Detroit 2.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Adkins, Onan Charles ⊕ Indianapolis; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; served in France during World War I; died May 26, aged 81, of myocarditis.

Bassett, Alice Haley ⊕ Boston; Boston University School of Medicine, 1898; died April 10, aged 89, of pernicious anemia.

Betz, Jonathan Clymont, Baltimore; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1899; died in the Johns Hopkins Hospital May 20, aged 79, of chronic asthmatic bronchitis.

Bitter, Harry, Brooklyn; University of Arkansas School of Medicine, Little Rock, 1927; member of the Medical Society of the State of New York and the American Academy of General Practice; died in the Williamsburg General Hospital March 24, aged 57, of coronary thrombosis.

Breco, Joseph Gideon, Corpus Christi, Texas; Southwestern University Medical College, Dallas, 1905; an associate member of the American Medical Association; member of the Oklahoma State Medical Association; practiced in Ada, Okla.; died in the Spohn Hospital May 23, aged 80, of ruptured abdominal aortic aneurysm.

Butler, Harry Herbert, Brookline, Mass.; Boston University School of Medicine, 1919; formerly associated with the Veterans Administration; died in the Veterans Administration Hospital, West Roxbury, Boston, May 5, aged 76, of cancer.

Calcagni, Oscar Henry ⊕ Morrisville, Vt.; University of Vermont College of Medicine, Burlington, 1936; veteran of World War II; on the staff of the Copley Hospital; died in Burlington May 2, aged 49.

Caldwell, Joseph Ridgely, Short Creek, W. Va.; Rush Medical College, Chicago, 1896; an associate member of the American Medical Association; past-president and vice-president of the Ohio County Medical Society; fellow of the American College of Surgeons; formerly practiced in Wheeling, where he was a member of the city council; served on the staffs of the Ohio Valley General and Wheeling hospitals in Wheeling; died June 7, aged 85.

Carnett, William Wallace, Formosa, Ark. (licensed in Arkansas in 1903); died in Little Rock May 22, aged 89.

Caswell, Harlow Orton ⊕ Jefferson, Wis.; Rush Medical College, Chicago, 1897; headed the county draft board during World Wars I and II and received a citation from President Roosevelt for his work; surgeon for the Northwestern Railroad; on the honorary staff, Fort Atkinson (Wis.) Memoria Hospital; assistant resident physician at the Jefferson County Hospital; died May 12, aged 84, o coronary thrombosis.

Civins, Albert Isaac, Cleveland; University o Wooster Medical Department, Cleveland, 1901 died May 16, aged 81, of cancer of the colon and liver.

Collier, Casa ⊕ Memphis, Tenn.; Northwestern University Medical School, Chicago, 1910; fellow of the American College of Surgeons; veteran of World War I; died May 11, aged 72.

Conkey, Ogden Fethers, Canton, N. Y.; Columbia University College of Physicians and Surgeons New York City, 1912; at one time on the faculty of Cornell University Medical College in New York City; died June 2, aged 72, of cerebral hemorrhage.

Conner, Elwin Kerr ⊕ Filer, Idaho; University of Nebraska College of Medicine, Omaha, 1954; certified by the National Board of Medical Examiners; died in the Bishop Clarkson Memorial Hospital, Omaha, May 3, aged 30, of cancer of the pancreas.

Cooley, Samuel Studdiford ⊕ Black Mountain, N. C.; University and Bellevue Hospital Medical College, New York City, 1934; specialist certified by the American Board of Internal Medicine; member of the American Trudeau Society; veteran of World War II; served on the staffs of the Memorial Mission Hospital of Western North Carolina in Asheville, Fellowship Sanatorium of the Royal League, and the Western North Carolina Sanatorium; died in Asheville May 9, aged 52, of coronary thrombosis.

Cornell, John Cecil ⊕ St. Louis; St. Louis University School of Medicine, 1909; served overseas during World War I; on the staff of St. Anthony's Hospital; died May 17, aged 71, of cancer.

Corrigan, Patrick Henry ⊕ Trenton, N. J.; born in Newark, Dec. 18, 1900; Georgetown University School of Medicine, Washington, D. C., 1923; past-president of the Mercer County Medical Society; secretary of the New Jersey Board of Medical Examiners; member of the Association for Research in Nervous and Mental Disease; specialist certified

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⊕ Indicates Member of the American Medical Association.

by the American Board of Internal Medicine; a trustee of the Medical-Surgical Plan of New Jersey; consultant, F. W. Donnelly Memorial Hospital and the Orthopaedic Hospital and Dispensary; on the staff of St. Francis Hospital, where he died May 28, aged 57, of myocardial infarction, and hypertensive cardiovascular disease.

Cowan, Clyde Robert ✠ Buzzards Bay, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1915; College of Physicians and Surgeons, Boston, 1917; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; for many years practiced in Boston; died May 10, aged 74.

Cremin, Lawrence Dennis, Riviera Beach, Fla.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore. 1914; veteran of World War I; died in the Veterans Administration Hospital in Coral Gables, April 1, aged 71, of carcinoma of the colon with metastases.

Damiani, Pasquale George ✠ Peru, Ind.; Hahnemann Medical College and Hospital of Philadelphia, 1925; formerly practiced in Philadelphia, where he was on the faculty of his alma mater, and on the staffs of the Hahnemann and Women's Homeopathic hospitals; chief of staff, Dukes-Miami County Hospital; died May 19, aged 58, of coronary thrombosis.

Davidson, Edward Young ✠ Washington, D. C.; Columbian University Medical Department, Washington, 1894; in 1916 president of the Medical Society of the District of Columbia and was instrumental in the planning and erection of its present building, where his portrait now hangs; in 1941 was awarded the society's Order of Merit for the most worthwhile contribution to the society and in 1929 it recognized his services by establishing the Davidson Lecture; died in the Eastern Star Masonic Home May 22, aged 97, of carcinoma of the colon.

Dawley, Walter Averill ✠ Rapid City, S. D.; University of Illinois College of Medicine, Chicago, 1926; fellow of the American College of Surgeons; immediate past-president of the South Dakota Cancer Society; served as a member of the school board; associated with the Homestead Hospital in Lead and Bennett Memorial and St. John's McNamara hospitals; died May 30, aged 58, of cerebral hemorrhage.

De Bell, Arthur Wise, Malden, W. Va.; University of the South Medical Department, Sewanee, Tenn., 1903; veteran of World War I; died May 22, aged 84.

Denton, Aulsey Leo, Castalia, N. C.; Medical College of Virginia, Richmond, 1918; veteran of World War I; died April 9, aged 68, of pulmonary emphysema, chronic bronchitis, and esophageal stenosis.

Denyes, Orville Leston ✠ Momence, Ill.; Chicago Medical School, 1931; veteran of World War II; on the staff of St. Mary's Hospital in Kankakee; surgeon for the Chicago and Eastern Illinois Railroad; died May 30, aged 57, in an automobile accident.

De Weese, Charles W., Livermore, Ky.; Hospital College of Medicine, Louisville, 1906; veteran of the Spanish-American War; died May 16, aged 77, of a heart attack.

Dickinson, Marion Franklin, Little Rock, Ark.: University of Arkansas School of Medicine, Little Rock, 1919; died May 18, aged 79, of cancer.

Dohm, Arthur J., St. Paul; Minneapolis College of Physicians and Surgeons, medical department of Hamline University, 1906; served as police surgeon; died in the Miller Hospital May 14, aged 77, of ventricular fibrillation and coronary sclerosis.

Donnelly, Leo Charles, Detroit; Detroit College of Medicine, 1911; died in Dansville, Mich., May 30, aged 68.

Dupras, Joseph Elzear, Auburn, Maine; Laval University Faculty of Medicine, Quebec, Que., Canada, 1906; member of the staff of the Central Maine General Hospital; died May 15, aged 77.

Eifert, Elmer Ernest ✠ Alfordsville, Ind.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1907; veteran of World War I; on the staff of the Daviess County Hospital in Washington, where he died May 13, aged 73, of pernicious anemia.

Elarbee, George Wiley ✠ Pahokee. Fla.; Atlanta College of Physicians and Surgeons, 1900; on the staff of the Everglades Memorial Hospital; died in West Palm Beach May 26. aged 82. of intestinal obstruction.

Emy, Saburo ✠ New York City; University and Bellevue Hospital Medical College, New York City, 1922; member of the American Society of Anesthesiologists; veteran of World War I; director of anesthesiology at the Misericordia Hospital, where he died May 20, aged 68, of cancer.

Etheridge, Carl Eugene ✠ Tuscaloosa, Ala.; University of Arkansas School of Medicine, Little Rock. 1929, on the staff of the Bryce Hospital; died in the Methodist Hospital, Rochester, Minn., May 21, aged 57, of cancer of the esophagus.

Fasting, George Frederick Christopher ✠ New Orleans; Rush Medical College, Chicago, 1926; served on the faculty of Louisiana State University School of Medicine; senior bacteriologist at Charity Hospital; died May 26, aged 66, of acute myocardial infarction.

Field, Martin Thomas ⊕ Salem, Mass.; Harvard Medical School, Boston, 1901; fellow of the American College of Surgeons; served as city physician and member of the health board; consultant at Salem Hospital; died May 22, aged 82.

Fine, Abraham, Woodmere, L. I., N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1906; veteran of World War I; formerly associated with the Mount Sinai Hospital in New York City; died June 4, aged 76.

Foust, Earl William ⊕ Royal Oak, Mich.; Detroit College of Medicine and Surgery, 1928; veteran of World War II; served on the staff of the Mount Carmel Mercy Hospital, Detroit, where he died May 19, aged 59.

Gale, Joseph, Miami Beach, Fla.; University of Illinois College of Medicine, Chicago, 1923; died May 14, aged 60, of cirrhosis of the liver.

Gantz, Frank Elwin ⊕ Washington, D. C.; George Washington University School of Medicine, Washington, 1926; member of the Industrial Medical Association; veteran of World War I; died in the Doctors Hospital May 23, aged 61, of cancer of the prostate.

Geis, Neil Charles ⊕ Chicago; Chicago College of Medicine and Surgery, 1913; member of the staff of Ravenswood Hospital; died June 3, aged 70.

Geraci, Frank Paul ⊕ Cleveland; Western Reserve University School of Medicine, Cleveland, 1917; fellow of the American College of Surgeons; veteran of World War I; on the staff of the Grace, St. Alexis, and Huron Road hospitals; died May 7, aged 66, of coronary thrombosis.

Gilmore, Rowland Thomas S. ⊕ Bemidji, Minn.; Trinity Medical College, Toronto, Ontario, Canada, 1895; fellow of the American College of Surgeons; died in Durand April 14, aged 88.

Giuliana, Robert Amedeo ⊕ Newark, N. J.; Long Island College Hospital, Brooklyn, 1898; served as president of the Physicians' Art Association of New Jersey; associated with the St. James Hospital, of which he was one of the founders; on the staffs of the Monmouth Memorial and Hazard hospitals in Long Branch and St. Vincent's Hospital in Montclair; died in Monmouth Beach May 28, aged 80, of coronary occlusion.

Gliedman, Lester Howard ⊕ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1950; assistant professor of psychiatry at his alma mater; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association; veteran of World War II; associated with the Johns Hopkins Hospital; died May 20, aged 39, in a plane crash.

Gordon, John Kyle, Chambersburg, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1904; an associate member of the American Medical Association; for many years member and president of the school board; on the staff of the Chambersburg Hospital; died May 20, aged 80, of carcinoma of the colon.

Grandfield, Robert Francis, Millis, Mass.; Middlesex University School of Medicine, Cambridge, 1927; died in the Framingham Union Hospital in Framingham May 17, aged 61, of cerebral thrombosis.

Gray, William Harry, Broadwater, Neb.; Lincoln Medical College of Cotner University, 1904; died May 7, aged 82, of diabetes mellitus.

Griffith, Mose Simpson ⊕ Galesburg, Ill.; Miami Medical College, Cincinnati, 1907; veteran of World War I; associated with Cottage Hospital and St. Mary's Hospital, where he died May 4, aged 74.

Guinan, Edward Robert, Los Altos, Calif.; Cooper Medical College, San Francisco, 1911; an associate member of the American Medical Association; fellow of the American College of Surgeons; member of the American Academy of General Practice; served during World War I; later served in the regular Navy; for many years chief of staff of Richmond (Calif.) Hospital; died in the Palo Alto (Calif.) Hospital May 26, aged 69, of congestive heart disease and pneumonia.

Hanes, Charles Benjamin ⊕ Ambler, Pa.; Jefferson Medical College of Philadelphia, 1947; interned at the Chestnut Hill Hospital in Philadelphia, where he served a residency and where he died May 30, aged 35, of injuries received in an automobile accident.

Hannum, Edwin Alan, Birmingham, Mich.; University of Wooster Medical Department, Cleveland, 1904; formerly practiced in Cleveland, where he was on the staff of the Lakeside Hospital; died in St. Joseph's Mercy Hospital, Pontiac, May 22, aged 85.

Harnett, David Louis ⊕ Chicago Heights, Ill.; Northwestern University Medical School, Chicago, 1926; member of the Aero Medical Association and the Industrial Medical Association; veteran of World War I; on the staff of the St. James Hospital; died in the Edgewater Hospital, Chicago, May 27, aged 63, of perforated gastric ulcer.

Herbert, Howard Beaman, Chicago; Chicago Medical School, 1933; member of the American Academy of General Practice; died in the Michael Reese Hospital June 8, aged 60, of myocardial infarction and coronary arteriosclerosis.

Herkimer, Daniel Robert ⊕ Lincoln Park, Mich.; Detroit College of Medicine and Surgery, 1927; member of the American Fracture Association; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World Wars I and II; served on the staffs of the William Booth Memorial and Mount Carmel Mercy hospitals in Detroit, Wyandotte (Mich.) General Hospital, Oakwood Hospital, Dearborn, and Outer Drive Hospital; for many years health officer; died May 11, aged 62, of acute right ventricular failure.

Herweg, Janet Ruth Scovill, Brentwood, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1943; certified by the National Board of Medical Examiners; interned at Barnes Hospital, St. Louis, where she served a residency; served a residency at St. Louis Children's Hospital in St. Louis; died in the Barnes Hospital, St. Louis, May 11, aged 39, of cancer.

Hudack, Stephen Sylvester ⊕ Enumclaw, Wash.; born in Cleveland Aug. 1, 1900; Western Reserve University School of Medicine, Cleveland, 1929; served as assistant clinical professor of surgery at his alma mater; at one time instructor in surgery and associate professor of orthopedic surgery at Columbia University College of Physicians and Surgeons in New York City, where he served in many capacities at the Presbyterian Hospital; director and founder of research in the division of surgery at St. Luke's Hospital in Cleveland; since September, 1957, surgical consultant at the Community Memorial Hospital; veteran of World War II; fellow of the New York Academy of Medicine and the American College of Surgeons; member of the Harvey Society, American Society for Experimental Pathology; American Association for the Surgery of Trauma, American Association for the Advancement of Science; died May 13, aged 57, of coronary occlusion.

King, Edward Philip ⊕ Chicago; Loyola University School of Medicine, Chicago, 1926; veteran of World War II; on the staff of St. Anne's Hospital; died June 6, aged 58, of acute myocardial infarction.

Kirschbaum, Arthur, Houston, Texas; born in New York City Oct. 15, 1910; University of Minnesota Medical School, Minneapolis, 1943; professor and chairman of the department of anatomy at Baylor University College of Medicine and the University of Texas Dental Branch; teaching assistant in zoology at his alma mater from 1931 to 1934, teaching fellow of anatomy from 1934 to 1937, instructor, 1941-1942, assistant professor from 1942 to 1945, and associate professor of anatomy from 1945 to 1951; instructor of anatomy at Yale in New Haven, Conn., 1938-1939 and 1940-1941; professor and head of the department of anatomy at the University of Illinois College of Medicine in Chicago from 1951 to 1954; member of the American Association for Cancer Research and secretary of the Southwest Section; member of the American Society for Experimental Pathology, International Association for Dental Research, Sigma Xi, Phi Beta Kappa, and the American Association for the Advancement of Science; in 1951 recipient of the Minnesota State Award of the American Cancer Society; recently appointed professional member of the National Advisory Health Council of the National Institutes of Health; consultant for the U. S. Public Health Service; consulting experimental hematologist for the University of Texas, M. D. Anderson Hospital and Tumor Institute; consultant, Veterans Administration Hospital; served as an advisory editor of *Cancer Research;* died in the Methodist Hospital May 28, aged 47, of myocardial infarction.

Knutson, Anton ⊕ Reynolds, Ill.; Chicago College of Medicine and Surgery, 1941; served on the staff of the Lutheran Hospital in Moline; accidentally drowned while fishing in Parent Lake, in Northern Minnesota, May 25, aged 73.

Laszlo, Daniel, New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1926; member of the Medical Society of the State of New York; specialist certified by the American Board of Internal Medicine; fellow of the American Association for the Advancement of Science; member of the American Association for Cancer Research; chief of the division of neoplastic diseases at Montefiore Hospital; died June 1, aged 55.

Learoyd, Charles Berry ⊕ Danvers, Mass.; College of Physicians and Surgeons, medical department of Columbia College, New York City, 1887; died in Waltham May 13, aged 98, of bronchopneumonia.

MacKinlay, Edgar Harold ⊕ McConnellsburg, Pa. Columbia University College of Physicians and Surgeons, New York City, 1929; certified by the National Board of Medical Examiners; director of public health of Fulton County; for many years county coroner; president of the First National Bank; on the staffs of the Fulton County Medical Center in McConnellsburg and Chambersburg (Pa.) Hospital, where he died May 10, aged 53, of cancer.

Martin, William S. ⊕ Memphis, Tenn.; Meharry Medical College, Nashville, Tenn., 1907; owner of the Memphis Red Sox Baseball Club and Martin Stadium; president of the medical staff and for many years superintendent of the Collins Chapel Correctional Hospital, where he died May 17, aged 78.

Masucci, Alberico ⊕ Paterson, N. J.; Boston University School of Medicine, 1930; fellow of the American College of Surgeons; on the staff of St. Joseph's Hospital; died April 18, aged 50, of asthma and an anaphylactic reaction following a third injection of "anti-polio vaccine."

Melzer, Fred John, Cleveland; University of Wooster Medical Department, Cleveland, 1908; served on the staff of the Polyclinic Hospital; died in the Mound Park Hospital, St. Petersburg, May 8, aged 71, of bronchogenic cancer.

Otis, Frank Jesse ⊕ Moline, Ill.; born in San Jose, Calif., April 22, 1873; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1899; Rush Medical College, Chicago, 1908; served on the faculty of the American Medical Missionary College in Battle Creek, Mich., and Chicago; fellow of the American College of Surgeons; formerly on the staff of the Battle Creek (Mich.) Sanitarium; at one time physician in charge of the Tri-City Sanitarium; associated with the Lutheran and Moline Public hospitals in Moline and the St. Anthony's Hospital in Rock Island; died in Loma Linda, Calif., May 8, aged 85, of acute coronary occlusion.

Parker, Carl Horace, Carmel Valley, Calif.; Rush Medical College, Chicago, 1909; specialist certified by the American Board of Radiology; an associate member of the American Medical Association; member of the American Roentgen Ray Society; formerly practiced in Pasadena, where he was on the staff of the Collis P. and Howard Huntington Memorial Hospital; died in Pasadena May 8, aged 75, of acute myocardial infarction.

Patton, Mathew Morrison ⊕ Spokane, Wash.; Northwestern University Medical School, Chicago, 1907; specialist certified by the American Board of Pathology; member of the College of American Pathologists; past-president of the Pacific Northwest Society of Pathologists; on the staff of the Sacred Heart Hospital; died in the Deaconess Hospital May 10, aged 78, of arteriosclerosis.

Pentecost, James Biggars, Winters, Texas; Southwestern University Medical College, Dallas, 1906; served as city health officer; died in the Hendrick Memorial Hospital, Abilene, May 11, aged 87, of angina pectoris.

Phillips, Clovis Hamilton ⊕ Cleveland; University of Cincinnati College of Medicine, 1929; specialist certified by the American Board of Obstetrics and Gynecology; veteran of World War II; served on the faculty of Western Reserve University School of Medicine; associated with Lakeside and Veterans Administration hospitals; died in Rye Beach, N. H., May 29, aged 55, of cancer of the esophagus.

Presser, Karl ⊕ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1924; served on the staffs of the Beth Israel Hospital in Boston and the Montefiore Hospital; died in the Mount Sinai Hospital May 25, aged 59, of cancer.

Ryan, James Bernard ⊕ Easthampton, Mass.; Tufts College Medical School, Boston, 1920; veteran of World War I; served for three terms as medical examiner for the Second Hampshire District from Massachusetts; school physician in Easthampton and Southampton; medical adviser of the medical care plan of the Easthampton Welfare Department; on the courtesy staffs of the Cooley Dickinson Hospital in Northampton and the Providence Hospital in Holyoke; died May 13, aged 61, of coronary thrombosis.

Sabatini, Felix Raphael, New York City; Fordham University School of Medicine, New York City, 1921; member of the Medical Society of the State of New York; died May 4, aged 61, of coronary thrombosis.

Schwing, Harold Edward ⊕ Sacramento, Calif.; University of Buffalo School of Medicine, 1923; member of the American Academy of General Practice and the Industrial Medical Association; member of the Mercy Hospital staff; died May 18, aged 63.

Shick, Mary McDowell, Elwyn, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1895; an associate member of the American Medical Association; for many years associated with the Elwyn Training School, where she died May 23, aged 92, of cancer.

Slabey, John Martin ⊕ New York City; Denver College of Medicine, 1898; served on the staffs of the St. John's, Gotham, and Medical Arts Center hospitals; died May 25, aged 81, of pulmonary infarction.

Tchertkoff, Iekoussiel G., New York City; Universite de Paris Faculte de Medecine, France, 1913; associated with Sea View Hospital in Staten Island and the Metropolitan Hospital; died June 1, aged 73, of myocardial infarction.

Wallace, Louis Osgood Sanborn ⊕ Manchester, N. H.; Maryland Medical College, Baltimore, 1912; member of the Association for Research in Nervous and Mental Disease; fellow of the American College of Physicians; veteran of World War I; suffocated May 20, aged 70, when his home was destroyed by fire.

Walter, Earle Charles, Mayfield, Ky.; Vanderbilt University School of Medicine, Nashville, Tenn., 1919; for many years associated with the Mayfield Hospital, where he died May 13, aged 63, of intestinal obstruction.

Ward, Michael Walter, Bangor, Wis.; Wisconsin College of Physicians and Surgeons, Milwaukee, 1904; served as president of the La Crosse County Medical Society, president of the village, president of the school board, and director of the Bangor Telephone Company; on the staff of St. Mary's Hospital in Sparta; died May 13, aged 80, of heart disease.

FOREIGN LETTERS

INDIA

Benactyzine in Psychoneurosis.—N. S. Vahia and co-workers (*Indian Journal of Medical Sciences,* vol. 12, February, 1958) treated 28 psychoneurotic patients with benactyzine, an anticholinergic drug with mild atropine-like action. All were treated as outpatients. Most were diagnosed as having an anxiety state or a psychogenic headache. They were given one 1-mg. tablet three times a week for the first two weeks followed by two tablets three times a day for a further period of one week. An immediate subjective improvement was observed. More than 25% improvement was seen in eight patients on a dosage of 1 mg. three times a day and in six patients on a dosage of 2 mg. a day. Benactyzine therapy was stopped in one patient because of worsening of symptoms. An increase of dosage from 3 to 6 mg. per day did not produce any significant improvement in the results. With 3 mg. a day, no toxic manifestations were noted; but on the increased dosage, patients complained of giddiness, which was so marked in one case that the use of the drug had to be discontinued.

Hyaluronidase for Dermatoses.—B. B. Gokhale (*Indian Journal of Dermatology and Venereology,* vol. 24, Jan.-March, 1958) observed that the cellular infiltration and reactionary growth of connective tissue that occurs in the chronic lesions of some dermatoses is in a large measure responsible for their chronicity. To overcome this factor, the author tried local injections of hyaluronidase in conjunction with certain other drugs in a series of 11 patients (2 with lichen planus hypertrophicus or verrucosus, 1 with sycosis muchae, 2 with lupus vulgaris verrucosus of the hands and feet, 2 with lichen simplex, one with pigmented circumscribed patches, and 3 with tuberculoid leprotic macules). They were given local injections of 150 units of hyaluronidase dissolved in 1 or 2 cc. of isotonic saline solution. These injections were painful even when a 2% procaine solution was used as the solvent. The injections were given once a week or once in two weeks, the usual course of treatment being 8 to 12 injections depending on the nature and size of the lesion. In addition to the hyaluronidase, 500,000 units of penicillin, 0.5 Gm. of streptomycin, 0.5 cc. of ethyl ester of hydnocarpus oil for the first injection and then increasing by 0.25 cc. for every following injection, or calcium-PAS in doses of 0.5 to 1 cc. of a 10% solution was injected. Eight of the patients showed a satisfactory result. One patient with lupus vulgaris developed an abscess which was incised and the final result was satisfactory. Two developed bullae on the treated areas, one being a patient with a tuberculoid leprotic macule and the other a patient with a chronic pigmented patch of 10 years' duration. On the whole the results were satisfactory clinically and cosmetically.

Hypoglycemic Action of Toluylene.—P. S. Haranath and co-workers (*Indian Journal of Medical Sciences,* vol. 12, February, 1958) studied the blood sugar–reducing properties of pure substances derived from some indigenous drugs and their synthetic analogues. One of these, Pterocarpus marsupium, is reputed to possess antidiabetic properties. One of the authors extracted pterotoluylene in a pure state from the heartwood of Pterocarpus marsupium, which was found to have a hypoglycemic action. A synthetic analogue of this drug was also prepared, and the actions of these two compounds was studied on the fasting blood sugar in dogs. Both the compounds being sparingly soluble in water, alcoholic solutions were prepared for intravenous injection and the blood sugar level determined before and at frequent intervals after the injection of the drug. Pterotoluylene produced a fall in blood sugar of 26 to 50% on intravenous administration in a dosage of 10 mg. per kilogram of body weight. Larger doses (20, 30, and 50 mg. per kilogram of body weight) reduced the blood sugar after an initial period of hyperglycemia. This fall lasted longer than the five-hour observation period. The synthetic analogue was also found to possess a hypoglycemic action on intravenous administration in doses of 0.5 to 2.0 mg. per kilogram of body weight. Larger doses (4 or 5 mg. per kilogram of body weight) reduced the blood sugar level after an initial rise.

Thus both the compounds showed a hypoglycemic action in smaller dosage, while with a larger dosage there was an initial period of hyperglycemia. The mode of this action is not clear. The action was more marked with pterotoluylene than with the synthetic compound. The blood pressure was reduced by pterotoluylene given intravenously to anesthetized dogs. This action was not abolished by vagotomy, atropinization, or administration of antihistamines. With larger doses, apnea and increased rate of respiration were seen. The splenic volume was reduced. Pterotoluylene in larger doses

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The items in these letters are contributed by regular correspondents in the various foreign countries.

proved toxic to two dogs who died at the end of 12 and 36 hours respectively after an initial period of listlessness and profuse salivation followed by dyspnea. With smaller doses no toxic effects were noticed in dogs at the end of the 10-day observation period.

Smallpox and Cholera.—The Union Health Ministry recommended to state governments investigation of the causes of the recent rise in the incidence of smallpox and cholera. The government of India has also requested the Indian Council of Medical Research to set up an expert committee for a similar purpose. The Health Ministry recommended that (1) the state governments consider whether the present system of registration of births in rural areas is satisfactory, as nonregistration of all live births results in the escape of many infants from primary smallpox vaccination; (2) revaccination be made compulsory; and (3) the reliability of the smallpox vaccine being used be investigated. Irregularity of the supplies also interfered with the satisfactory working of the vaccination program. Regarding cholera, the ministry recommended stockpiling of the necessary anticholera drugs, disinfectants, and water sterilizing agents; regular disinfection of all sources of water supply three weeks prior to the usual cholera season and thereafter at regular intervals; strict control over sanitation in fairs and festivals and compulsory inoculation of all persons attending these; and enforcement by all municipalities of sanitary regulations during this period.

Blood Histamine in Peptic Ulcer.—Basu Malik and Bhattacharya (*J. Indian M. A.* 30:9 [May 1] 1958) studied a series of 20 patients with chronic peptic ulcers to determine whether there is any correlation between the basal acid secretion and the blood histamine level. The diagnosis in these patients was confirmed by roentgenography, and the blood was collected when the disease was in the active stage. The level in all these patients except one was found to be within the normal range, varying from 1 to 8 mcg. per 100 ml. In only one was the value high (17.5 mcg. per 100 ml.). No correlation could be found between the blood histamine level and the basal acid secretion of gastric juice.

Tolbutamide.—N. J. Mody (*J. A. Physicians India* 6:2 [April] 1958) stated that tolbutamide had a marked hypoglycemic action in both diabetic and normal persons. In the treatment of properly selected diabetics it has a definite place. The best method of assessing the orally given hypoglycemic drugs is to study three-hourly blood sugar patterns with and without the drug, as these give a better idea about the action of the drug than studying only the glucose tolerance. Of his 22 patients 6 were receiving carbutamide prior to the trial. One of these developed intolerance to carbutamide and was therefore changed over to tolbutamide therapy, and one, though fully controlled by carbutamide, failed to respond to tolbutamide. Eighteen patients were between 40 and 60 years of age, two were below 40 (25 and 30), and two were over 60. One patient put on 6 lb. after treatment with tolbutamide and another lost 6 lb. Both were well controlled by the drug.

Each patient's diet was studied and adjusted after admission according to the desired weight for his height. Fourteen had taken 20 to 80 units of insulin daily. Nine had a family history of diabetes. Tolbutamide was started after about five days of hospitalization and dietary adjustment; 4 Gm. were given in four equal doses on the first day followed by 3, 2.5, and 2 Gm. on successive days. Six patients were fully controlled by this regimen. Their average fasting blood sugar level was 227 mg. per 100 cc., and the average after therapy with the drug was 105 mg. per 100 cc. One of these patients was an obese woman aged 65 years with a diabetes of 15 years' duration. Her condition was previously controlled with carbutamide, but tolbutamide was substituted because she developed an itching rash. The rash disappeared, and the disease was kept under control with tolbutamide. No side-effects were noticed in any of the patients. Seven who had a more advanced diabetes than the six mentioned above, with an average fasting blood sugar of 242 mg. per 100 cc., had a fair result, the average fasting blood sugar level after treatment coming down to 152 mg. per 100 cc. Nine patients were not benefited. Two of these had juvenile diabetes.

Another patient, also a juvenile, responded fairly well to tolbutamide. The average fasting blood sugar in this last group was 207.6 mg. per 100 cc. before treatment and 137.5 mg. per 100 cc. after treatment. No side-effects were noticed in any of these patients except one who complained of giddiness. There was no evidence of euphoria, and one patient complained of a sense of depression. The renal threshold was not affected by the drug. As compared to therapy with carbutamide, that with tolbutamide required a slightly larger dose, and it had to be given at more frequent intervals. The drug acted well in patients with recent as well as with old diabetes, obese or otherwise, and in diabetics above the age of 40. Rigid dietary control is, however, essential.

Vaginal Moniliasis.—S. C. Pandya and co-workers (*J. Indian M. A.* 30:9 [May 1] 1958) studied the action of nystatin vaginal tablets in the treatment of 36 patients with vaginal moniliasis. The diagnosis was based on clinical evidence of vulvovaginitis, characteristic vaginal discharge, microscopic evidence of the presence of yeast cells in the discharge, and demonstration of Candida albicans in the discharge. All the patients had a history of increasing vaginal discharge, which was of short duration in 19, present for over two months in nine, and present for over a year in 8. Thirty-four complained of itching around the anus, and 33 had burning on micturition. Six complained of a constant dull pain in the lower abdomen. Eight were nulliparas, 9 primiparas, and 19 multiparas. Twenty-four patients were receiving a nutritionally poor diet. The pH of the vaginal discharge was between 5 and 5.9 in 2 patients, between 6 and 6.9 in 30, and 7 in one. Thirty-two patients were treated with nystatin vaginal tablets. Half of them used one and the other half used two tablets at bedtime. One patient treated for six days with one tablet a day showed complete recovery during this period. Microscopically, the fungus could not be detected after the 12th day, and there was no relapse for at least nine weeks.

Twelve patients used one tablet a day for 8 to 14 days. Complete recovery resulted in all cases within 14 days, and microscopic evidence of cure was obtained between the 13th and 19th days. Of these, 10 patients did not relapse and the 2 who did responded to retreatment with nystatin. Five patients were treated with one tablet a day for 18 to 20 days. Complete clinical recovery occurred during this period, and cultures remained negative from the 20th day onwards. Fourteen patients used two tablets a day for one to two weeks. All were symptom-free in two weeks, and cultures were negative after the 14th to 20th day. No relapse occurred in 10 of these patients. Two patients received two tablets for 15 to 18 days each. Both were clinically cured, and cultures were negative after three weeks. There was no relapse. Thus best results were obtained with a treatment of about two weeks. The results also showed that treatment with one tablet a day was just as effective as with two tablets a day. The authors recommended the larger dosage in patients in whom the condition was severe or there were such complicating factors as diabetes or pregnancy. No change in the pH of the vaginal discharge was observed after successful treatment.

Electrophoretic Profile in Hematological Disorders. —V. B. Mitbander and co-workers (*Indian Journal of Medical Sciences,* vol. 12, Feb., 1958) studied the alterations in plasma proteins in 28 patients with hematological disorders. The plasma proteins were also determined in seven healthy adults between the ages 20 and 35 who served as controls. The percentages of α_1-globulin for the normal subjects were lower and those for V factor and fibrinogen higher than the percentages reported from other countries. A decrease in the albumin and β-globulin and an increase in the α_1-globulin were observed in patients with chronic granulocytic leukemia. This is slightly different from the readings reported by other authors, who did not find any alteration in the albumin level. The decrease in the albumin in the present series may be due to the poorer nutritional status and hypoalbuminemia of these patients. In patients with chronic lymphocytic leukemia, the albumin level showed reduction while the α_1-globulin was increased. The other protein fractions showed individual variations. In a patient with anemia due to ancylostomiasis, the albumin level was lowered and all the globulin components were increased. In another patient with refractory anemia, all the plasma proteins were diminished except α_1-globulin, which remained constant. Similar changes were seen in patients with acquired hemolytic anemia. In other patients with anemia there was a marked increase in α-globulins, fibrinogen, and V factor and a decrease in the albumin. In a patient with miliary tuberculosis all the plasma proteins were diminished except α_1-globulin, the reduction being most marked in albumin.

In a patient with severe anemia with tuberculosis, albumin and β-globulin were decreased and other fractions were increased. α_1- and α_2-globulins were markedly increased in a patient with Hodgkin's disease; the albumin and β-globulins were decreased and the fibrinogen and the V factor increased. There was the characteristic hyperproteinemia in a patient with multiple myeloma, the Bence-Jones protein appearing in the V factor fraction; the fibrinogen showed a striking reduction, the albumin was decreased, α-globulin was elevated, and β-globulin unaffected. In all patients with visceral leishmaniases, an interesting pattern was seen with a marked increase in the V factor, a marked decrease in albumin, a decrease in β-globulin, and an increase in fibrinogen and α_1-globulin. The V factor showed a sharp increase in patients with chronic cirrhosis; the α-globulins were increased and albumin and β-globulin decreased. The pattern was normal in a patient with paroxysmal nocturnal hemoglobinuria, the total proteins also being unaffected. A marked increase in fibrinogen and V factor was seen in a patient with atypical reticulosis with hemolytic anemia in whom the Coombs test was repeatedly negative. Thus the changes as noticed in this series were characteristic in patients with Hodgkin's disease, multiple myeloma, visceral leishmaniasis, and cirrhosis while in leukemia, anemia, and tuberculosis they were nonspecific.

Psoralens for Vitiligo.—B. N. Srivastava (*Indian Journal of Dermatology and Venereology,* vol. 24, Jan.-March, 1958) gave methoxsalen orally and locally to 100 patients with vitiligo, their ages varying from 2½ months to 51 years. Most of the patients were vegetarians, and some showed definite evidence of malnutrition and vitamin deficiency;

24 had varying grades of anemia, mostly of the hypochromic microcytic type, and 26 had eosinophilia. In only one was there oxyuriasis. One patient had a family history of asthma, and another had eczema. In others no cause for the eosinophilia was apparent. The drug was given orally in a daily dose of 0.7 mg. per kilogram of body weight and externally in a lotion. On an average, the treatment was started in adults with 10 mg. per day in the first week, and the dose was increased by 10 mg. every week till 40 mg. a day was reached. This was continued till therapeutic results were obtained. If toxic reactions appeared, the dose was reduced or omitted temporarily. The dosage was modified in children according to their weight.

To minimize severe local reactions, local treatment was started with a 1:4 dilution of a paint containing 0.18% of methoxsalen. Sometimes higher dilutions with 60% alcohol as the solvent were used. An ointment was used instead of the lotion in sensitive patients. The paint was applied to the affected area at night, and the painted area was exposed to sunlight the next morning for about one minute initially and subsequently for one to five minutes. It was then washed thoroughly to prevent overexposure. In this series 28 patients were cured, and the rest showed some improvement. The minimum time taken for complete cure was three weeks and the maximum two years. Patients in the younger age group and those with vitiligo of recent origin responded earlier. In two patients the disease advanced in spite of treatment. Side-reactions included actinodermatitis, headache, anorexia, burning sensation, gastroenteritis, oral and rectal bleeding, anemia, urticaria, and psychotic episodes. Higher dilutions of the drug than those used by Western workers were found to be effective. Severe actinodermatitis resulted when a solution of a strength similar to that used in the West was used. The time required for the onset of pigmentation and cure was also comparatively shorter.

Drug Resistance in Bacillus Subtilis.—Joshi and Sreenivasan (*Proc. Indian Acad. Sc.* 47:1 [Jan., section B] 1958) stated that the acquisition of resistance to a drug may sometimes be due to the organism developing an ability to detoxify the drug, involving the synthesis of an enzyme which is concerned in the destruction of the drug. They studied local strains of Bacillus subtilis to find out whether organisms that have become resistant to sulfonamides owe this property to detoxification by acetylation through the mechanism of an enzyme. The organisms were exposed to concentrations of sulfanilamide gradually increasing to 500 mg. per 100 ml. in the culture medium. Sulfanilamide was used in these experiments because it is acetylated to a greater extent than *p*-aminobenzoic acid, sulfathiazole, or sulfadiazine. The extent of acetylation was studied with the susceptible parent strain as well as with strains that were rendered resistant to 50 and 500 mg. per 100 ml. of sulfanilamide. The susceptible strain gave a scanty growth in the presence of the drug, requiring a longer incubation period. With the resistant strain, good growth was seen within 18 hours. The free and total sulfanilamide was estimated in these cases at the end of 24 and 72 hours, but there was no evidence of acetylation. With strains resistant to higher concentrations of sulfanilamide, a diazotizable arylamine was produced in the culture filtrate in large quantities even in the absence of any added sulfanilamide. This amine was not seen in control tubes which were sterilized after inoculation and then incubated simultaneously for varying lengths of time. Thus the mechanism of detoxification of sulfonamides by acetylation is not the one involved in the production of drug resistance by B. subtilis.

MEXICO

Congress of Obstetrics and Gynecology.—At the joint meeting of the Latin American Congress of Obstetrics and Gynecology and the Mexican Congress of Obstetrics and Gynecology in Mexico City in June, H. Rocamora, of Cuba, reported on the surgical risk during pregnancy. In cesarean sections his case fatality rate dropped from 6.9% (1934 to 1940) to 0.6% (1948 to 1956) due mainly to the use of antibiotics, transfusions, better anesthesia, and simpler surgical techniques. Infections and hemorrhages cause 84% of the maternal deaths. Segmental transperitoneal cesarean section with the patient under spinal anesthesia is to be preferred. The case fatality rate in ectopic pregnancy was 1.2%. Of the surgical complications of pregnancy, appendicitis was most common. Appendectomy was not attended by a higher case fatality rate in pregnant than in nonpregnant women. In 66% of the patients with ovarian tumors it was necessary to interrupt pregnancy. Cardiovascular operations were performed successfully in two pregnant women. Surgical complications of pregnancy are rare in Cuba, and the speaker operates on such patients only when absolutely necessary.

A. de Moraes, of Brazil, discussed the treatment of advanced genital cancer in women. In selected cases extraradical surgery may produce fairly long survival periods and even five-year cures. Radium and x-ray therapy should be attempted in all inoperable patients. The radioisotopes, specially radioactive gold, can be useful and complement treatment with cobalt-60. Chemotherapy gives poor results in women with advanced genital cancer. As an adjunct to treatment, hormones, especially testosterone, can be helpful. Castration, hypophysectomy, and adrenalectomy do not cure cancer, and their value is doubtful. N. Dias B., of El Salvador, reported a series of 1,485 patients with genital carcinoma; 1,318 of these had cervical carcinoma, 592 (44.9%) of which were advanced (stage 3 and 4). Extraradical surgery, radiation therapy, or a combination of both do not solve the problem of advanced genital carcinoma in women. Stage 3 cervical carcinoma should be treated primarily by radiation. Radical and extraradical surgery should be used only in selected cases or in the presence of radioresistance or recurrence. Irradiated patients should be kept under clinical, cytological, and histopathological observation to determine treatment in the later stages. Stage 4 carcinoma was treated by this speakers either by x-ray alone or by x-ray plus radium, with good palliative results. When there is involvement of the urinary bladder or the rectum, without fixation to the pelvis, an evisceration may be attempted. In the speaker's series, there were 38 cases of carcinoma of the vulva. Radical surgery in the operable patients showed that 50% had metastasis to pelvic lymph nodes, which indicates that vulvectomy should be accompanied not only by complete inguinal dissection but also by careful removal of the pelvic lymphatic system.

J. Noriega, of Mexico, stated that in his series, stage 3 carcinomas were treated with intrauterine radium and external irradiation, preferably with the cobalt bomb, aimed at the parametrial and lymphatic tissues. Stage 4 carcinomas were treated initially with external irradiation, with use of multiple small fields. According to the response, intrauterine radium might be applied. M. Briones P. and co-workers of Mexico discussed the physiopathological problems of the residual ovary. They concluded that ovaries should always be spared in young women, unless there is a clear indication for their removal. It is possible to save one or both ovaries, when they are healthy, and allow them an adequate blood supply, intact innervation, and good tubo-ovarian synergy. After 40 the incidence of tumors of the ovary increases. Although the incidence of such tumors may be as much as 21%, malignancy occurs in only 0.5%. Monthly checkups of women with residual ovaries are recommended for the first six months. After that checkups should be made at lengthening intervals, until they are made twice a year.

SWEDEN

Tissue Transplantations from the Dead.—With the growing practice of taking grafts from the skin, eyes, and bones of persons other than the recipients of them, the problem of ownership has come to the fore. The transfer is a comparatively simple matter from the legal aspect when both donor and recipient are alive, but surgeons have hesitated to help themselves to grafts from the dead when the transaction has not been legalized by some formal declaration on the subject from the prospective donor or his relatives. The parliament has now adopted legislation designed to facilitate the taking of grafts from the dead. The new law entitles certain hospital surgeons to help themselves to tissues taken from patients who have died in hospital or have been brought in dead. A safeguard against any abuse of this privilege is provided by a clause giving hospital patients or their nearest relatives the right to anticipate and prevent such action by forbidding it in advance.

State Mental Hospitals.—Debates in the Swedish Parliament continue to disclose the shortcomings of the state-managed mental hospitals which unfortunately do not share with Sweden's general hospitals in the reputation for being among the best in the world. More than a year ago, it was admitted in Parliament that in a mental hospital housing 669 patients there were only two attending physicians. Later figures covering the year 1956 showed that the average of overcrowding was 14%, though in certain hospitals it was 38%. In some of the older mental hospitals the patients must go to bed at 6 p. m. for want of personnel to look after them, and for want of proper lighting they cannot read in bed. Were funds available for new buildings to relieve the overcrowding, the lack of medical and subordinate staff would still be a serious obstacle, for over 63% of the junior hospital appointments are not filled or are held by temporary substitutes. A more optimistic note comes from the St. Lars hospital in Lund, where a locked wing for 65 violent women patients was thrown open and 39 patients are now engaged in occupational therapy thanks to the initiative of the medical superintendent and to modern drugs.

Specialization.—Of the 5,698 members of the Swedish Medical Association 3,318 have qualified as specialists. To enjoy the privileges conferred by specialization, they have had to fulfill various conditions before inclusion in the register kept for the purpose. Among the 26 different specialties there are several whose limitations are indicated by the paucity of exponents. Thus there are only six specialists in neurosurgery, six in disturbances of speech, and nine in plastic surgery. There are 21 in anesthesiology and 34 in diseases of the teeth. The most popular speciality is internal medicine with 783 qualified specialists. The surgeons and cardiologists come next with 491 and 264 respectively. Only 98 are neuropsychiatrists, whereas 222 are specialists in diseases of the lungs.

Influenza Epidemic.—Dr. Inga Rydén and coworkers (*Sevenka läkartidningen*, May 2, 1958) studied the outbreak of influenza that occurred in the fall of 1957. The epidemic showed no age or sex discrimination, the number of patients over 70 corresponding to the age distribution of the whole population. Among the 85 patients admitted to hospital were 35 with pneumonia which usually ran a comparatively mild course, with the temperature returning to normal in three to four days. The virus of the Far East type A was isolated from eight patients who died and from others who recovered. A vaccine made from this type was given in two injections to the 24 members of the hospital staff likely to be exposed to massive infection in the course of their work as the epidemic progressed. Of these 14 remained well, 7 had a mild attack, and 3 had to report sick. The patients developing pneumonia were given antibiotics, and when penicillin or streptomycin failed, chloramphenicol was tried. None of the patients given chloramphenicol had to resort to any alternative antibiotic.

Kidney Stones and Gallstones.—Dr. A. Fritjofsson (*Nordisk medicin*, May 22, 1958) made a statistical analysis of the 20-year period 1937-1956 during which about 8,900 patients with stone in the kidneys and ureters were treated in the local hospitals. A chart of this period showed a fairly steady rise in the number of such cases, but to discount the confusion due to the growth of the population, the figures were readjusted so as to present the number of these cases per 100,000 of the population. With this readjustment there was a rise from 460 in the first five years to 900 in the last five. Fritjofsson then quoted the findings of Edlund and Olsson who in 1956 published a study of the cholecystectomies carried out in Gothenburg during the 15-year period 1940-1954. They also took the precaution to calculate their numbers per 100,000 inhabitants and found that these numbers had more than tripled in 15 years. The reasons for these increases remain obscure.

Hospital Administration.—In recent planning for prospective hospital legislation, it was proposed that laymen should be put in charge of hospital administration on the assumption that in this respect they are more effective than members of the medical profession. This proposition led to a meeting last December at which the Swedish Medical Association and other bodies interested in hospital services were represented. It was agreed that medical administration was preferable to lay administration of such services and that it was desirable for doctors willing to discharge administrative hospital duties to qualify for them by special training. To this end it was agreed that such training should be made available for up to 20 trainees in May. The Swedish Medical Association has undertaken to contribute to the expenses of these trainees whose attendance at the short course of lectures in May may be supplemented later by a much more ambitious course of several weeks. This latest move is just one more protest against the teaching that medical men are unsuited by their training for administrative responsibility. To counter it effectively, the Swedish holders of senior hospital appointments are urged in the organ of the Swedish Medical Association not to trust to improvisation when taking on administrative duties, but to fit themselves for them by the educational facilities now available.

UNITED KINGDOM

Medical Ethics.—The General Medical Council is sending every physician a notice, reminding him of the major rules of his profession and the penalties for breaking them. The existing rules had not been amended since 1914, and as a result many physicians appear before the disciplinary committee of the council on charges not mentioned in the present notice. The new notice sets out offenses which raise questions of infamous conduct under the following main headings: (1) adultery, or improper conduct with a patient; (2) advertising and canvassing; (3) signing untrue or misleading certificates; (4) associating with unqualified practitioners, such as faith-healers; and (5) miscellaneous other items. Some members of the council have been worried about the increase in the number of physicians charged with offenses involving alcohol and at some trends in the issuing of medical certificates. The appearance of doctors on television has raised complex questions about advertising.

Assessment of Drug Action.—A symposium on quantitative methods in human pharmacology and therapeutics was held in the Wellcome Auditorium, London, in March. It was arranged by the coordinating Committee for Symposia on Drug Action of the Biological Council and was supported by the British Pharmacological Society, the Royal Society of Medicine, the Physiological Society, and the Biometric and Nutrition Society. In the session on the measurement of subjective states Prof. C. A. Keele said that the best way to measure pain and compare the effects of analgesic drugs was to rely on subjective assessments by the patient rather than to attempt to measure such physical accompaniments of pain as sweating, change in pulse rate, and wincing, as these are too variable. Dr. P. Sainsbury told how, by electromyography, he measured muscle tone, involuntary movements, fidgeting, and gestures in anxious patients as an index of anxiety.

Dr. H. Steinberg discussed the quantitative effect of drugs on intellectual performance, reasoning, memory, perception, and vigilance. The effect of drugs on performance may be either on incentive or on the actual ability to do the job. It is important to distinguish between the two. Drug responses may vary according to whether a subject knows whether he is doing well or badly in a test. Small degrees of anxiety act as an incentive, and it may be important that this should not be suppressed by drugs, or achievement may be hindered. Fortunately this problem is not socially urgent, as drugs are relatively ineffective in allaying anxiety without producing undesirable side-effects. The symposium was reported in the *British Medical Journal* for May 3.

Symposium on Clinical Trials.—A symposium on clinical trials was held at the Royal Society of Medicine (*British Medical Journal*, May 3, 1958). Dr. J. G. Scadding said one prerequisite was that extensive experiments on animals, and, sometimes, a few human volunteers had been carried out. A pilot trial might follow, and then a controlled trial. In some circumstances ethics would always make a therapeutic trial impermissible, because at all times the patient should be given the advantage of the best treatment available. Professor J. W. Crofton, after saying that the control group was in many respects the safest one to belong to, pointed out that in some situations no control group was required. This might be so during the testing of the treatment of a highly fatal acute disease, such as tuberculous meningitis with streptomycin, or the testing of a new drug with consistently dramatic results, such as chloramphenicol in scrub typhus. The physician taking part in the trial must have a "conscience clause" so that he can give his patient the best possible treatment regardless, if necessary, of the trial's requirements. Thus the results of treatment with many familiar substances are still not precisely known. Dr. Dudley Hart dwelt on the dangers of enthusiasm in the staff concerned in a therapeutic trial and showed how a "revivalist" atmosphere surrounding the introduction of a new method of treatment could not merely upset the recording of observations and the deductions to be made from them but could lead to the production of entirely misleading data by patients whose reactions to treatment sprang from a strong expectation of cure. Among the rules he set out for the careful control of a trial were: "Be disinterested," and "Consult a statistician beforehand."

Renal Damage by Mercurial Diuretics.—Mercurial diuretics are often given to patients with congestive heart failure irrespective of the state of the kidneys. Five cases of the nephrotic syndrome attributed to the use of mercurial diuretics over long periods were observed by Riddle and co-workers (*Brit. M. J.* 1:1274, 1958) who concluded that the syndrome is a definite risk in long-term mercurial diuretic therapy and that it may be more frequent than has hitherto been supposed. The diuretics used were mersalyl, Neptal chlormerodrin, and mercaptomerin. Two of the patients received weekly injections of mersalyl for three years. Three patients died, and although there was no previous history of renal disease, the clinical features and pathological findings were consistent with a nephrotoxic action of mercury. The urine was loaded with protein, the serum albumin level was low, and the serum cholesterol level raised. In the three fatal cases the macroscopic and microscopic appearance of the kidneys was the same. The cortices were swollen and were pale yellow-gray. The renal tubules showed necrosis, degeneration of the epithelium, and infiltration of the tubular cells with isotropic and anisotropic fat. Elsewhere cloudy swelling and hyaline droplet degeneration were observed. Tests for mercury in the kidney were strongly positive. The pathological changes resembled those seen in mercury poisoning. Increasing edema and increasing dyspnea were mistaken for a terminal exacerbation of chronic heart failure but were due to renal failure. Treatment with dimercaprol, corticotropin, and ion-exchange resins was of no avail. One patient recovered without specific therapy, suggesting that the condition is sometimes reversible. Early recognition of the condition and cessation of mercurial therapy before irreparable renal damage has occurred offers the best chance of recovery. The warning signs of the onset of the nephrotic syndrome are failure of proteinuria to decrease after a satisfactory diuresis, increasing edema, and absence of diuresis after injections of a mercurial diuretic. The first is the most useful sign.

Shoe-Fitting Fluoroscopes.—As a result of an agreement between the manufacturers of shoe-fitting fluoroscopes, the retail shoe trade, and the home office, the amount of radiation emitted by these machines was limited as of July 1. Each fluoroscope must bear a notice on it warning against over exposure, and existing machines that do not conform to regulations and emit more than the allowable degree of radiation must be modified. A notice on the machines will advise customers buying shoes not to have more than 12 shoe-fitting exposures a year. Operators trained in using them will see that each exposure is minimal. This approach by the manufacturers was prompted by a recent report by the Medical Research Council, which urged that the use of x-rays in shoe-fitting be abandoned except when necessary for orthopedic reasons.

Tetanus.—At a meeting at the Royal Society of Medicine, Professor Payling Wright of London explained how tracer techniques using labeled foreign proteins and fluorescent dyes enabled the fate of an injection of antitetanic serum (A. T. S.) to be followed. Such foreign proteins as tetanus-antitoxic horse globulins are removed from the circulation and destroyed more rapidly after the second or subsequent inoculation. The first dose of 1,500 units of A. T. S. confers protection for two or three weeks, but tracer studies show that the second dose disappears in a much shorter time. Professor Wright cited a case of tetanus occurring after the usual prophylactic dose of A. T. S. and recommended immunization against diphtheria and tetanus with the appropriate toxoid. Once a person has been injected with horse serum proteins, A. T. S. cannot be guaranteed to protect against tetanus, should exposure occur. Dr. D. Laurence deprecated the treatment of tetanus with drugs of unknown activity. Ideally any remedy should prevent spasms without blocking respiration or consciousness. Muscle spasms are best relieved by chlorpromazine and related compounds, which are better than muscle relaxants and centrally acting relaxants such as mephenesin. The best compound tested was acetylpromazine, although it has not been submitted to clinical trial yet. Relief of anxiety is essential in the management of tetanus.

Professor E. Adams, of Durban, reported a controlled clinical trial of chlorpromazine in nearly 200 patients with tetanus. His impression was that a mixture of barbiturates and chlorpromazine was better than either drug alone and enabled smaller doses of each to be given. In neonatal tetanus he preferred barbiturates. Chlorpromazine could be given intravenously and was of help in controlling laryngeal spasm. The total daily dose should not exceed 1 Gm. In assessing any new form of treatment, such prognostic criteria as period of onset and severity of spasms must be considered in each case. The earlier the onset the higher the mortality, and the less severe the spasms the lower the mortality. The cause of death is variable, but exhaustion from spasms is not a likely cause. Respiratory complications, hyperpyrexia, and circulatory failure are far more likely. Dr. A. C. Smith, of Oxford, said that new methods of treating tetanus had little effect in reducing mortality. At the Oxford Respiration Unit patients with spasms that could not be controlled by other means were given muscle relaxants and intermittent-pressure respiration. Four of seven recovered completely. Such a technique can only be carried out in specially equipped centers. Careful nursing and biochemical control are essential. This form of treatment could be carried out for three or four weeks if necessary.

Prognosis of Infectious Hepatitis.—Although it is generally agreed that most patients suffering from acute infectious hepatitis recover completely, with no lasting damage to the liver, few long-term follow-up studies had been made to confirm this impression. Cullinan and co-workers (*Brit. M. J.* 1:1315, 1958) followed up 1,405 men who had suffered from this disease in one of the four massive outbreaks of the disease that ravaged the armies massed around the Mediterranean Sea in World War II. Infectious hepatitis cost the British troops in the Middle East over 500,000 man-days in hospital. Most of the men were between the ages of 18 and 30 years, and the incidence in the officers was much greater than in men of other ranks. There were only four deaths from hepatic necrosis associated with the acute attack, a case fatality rate of 0.28%. Of the original 1,405 men, 91.6% were contacted. Recurrence of symptoms occurred in 8.3% of patients after leaving hospital at times varying from weeks to several years. About 26% felt completely fit immediately after leaving hospital: 68% at the end of a month, 87% at the end of three months, and 95% at the end of one year. The general pattern of illness in those who were not fit was one of malaise and digestive disturbance. Seven years after the attack 3.2% of the men complained that they had not felt well since the acute illness. They complained of periodic slight jaundice, persistent lassitude, intolerance of fat and alcohol, loss of appetite, nausea, depression, indigestion, and periodic vomiting. No deaths after the original illness and no cases of subacute necrosis leading to cirrhosis were recorded.

Factory Work in Mental Hospitals.—The Minister of Health and his staff are discussing ways of introducing industrial work in mental hospitals in order to accelerate the social rehabilitation of the patients. This followed a suggestion made by the Central Health Services Council in their annual report. The Medical Research Council has already set up workshops in mental hospitals, where selected patients have been given work contracted from neighboring factories. Schemes have been developed in 13 mental hospitals and 8 mental deficiency hospitals, with marked psychiatric and social benefit to the patients. The council's report recommends that the industrial projects in the hospitals be separate units, with normal working hours and conditions and standard factory pay rates. Working under conditions similar to those in industry should give the patients an incentive to reestablish themselves socially and encouragement to handle their own money and so regain the habit of looking after themselves.

Shortage of X-ray Technicians.—There is such a shortage of x-ray technicians at Walsall Hospital that two of them are having daily blood examinations because of the risk they run of excessive exposure to radiation. At an inquest on an elderly woman who died at the hospital while undergoing an emergency operation, it was stated that it was not possible to obtain an x-ray examination at the time owing to shortage of staff. Due to understaffing these technicians were overworked. The shortage is attributed to the long training required and the low salaries paid. A newly qualified technician receives $1,200 to $1,300 a year, with the expectation of a maximum of $1,600. The shortage is most acute in the smaller hospitals.

Death of Webb-Johnson.—Lord Webb-Johnson, former president of the Royal College of Surgeons and consulting surgeon to the Middlesex Hospital, died in London at the age of 77. When Dean of the Middlesex Hospital Medical School in the 1930's he was largely responsible for the rebuilding of the Middlesex Hospital. Great damage was done to the buildings of the Royal College of Surgeons in London in World War II, and during Lord Webb-Johnson's presidency of the college he was instrumental in expediting the rebuilding. New departments were established and professorial chairs were endowed for anatomy, pathology, and ophthalmology, and faculties in dental surgery and anesthesiology were established. In this he was helped by funds provided by Lord Nuffield, The Wellcome Trust, and a former patient.

Spiritual Healing.—Following swiftly on the heels of its counterpart in Scotland, as reported previously, the Church of England has published a report on spiritual healing. In this the view is expressed that the time is ripe for a *rapprochement* between the church and medicine. Medical science is laying increased emphasis on the unity of man's nature, recognizing more and more that the causes of much physical illness and mental disturbance are to be found in the deep and intimate relationship of the physical, mental, moral, and spiritual in man. In discussing public healing services, the report sees dangers inherent in large public demonstrations of healing and considers that these dangers are present even in the smaller and more carefully controlled public healing services held in parishes. It is recommended that in every diocese a panel of priests and physicians be set up under the authority of the bishops to advise the clergy in matters relating to the conduct of healing services. Further the clergy should do their utmost to secure the understanding, advice, and cooperation of the medical attendants of those to whom they minister. Persons seeking the ministrations of the church at a healing service should be advised to place themselves under the care of a physician if they have not already done so. The report commends to the attention of principals of theological colleges, deans of medical schools, and chaplains of teaching hospitals the recommendation of the British Medical Association, that the purpose of cooperation between the physician and the clergyman should be brought before medical and theological students by means of lectures and discussions.

On the subject of demonology, it was found that some form of exorcism is at present used in this country: infrequently in the case of persons, but less infrequently in the case of places. The great difficulty in detecting demons is stressed, and also the dangers inherent in the misuse of exorcism. The patient must therefore be carefully examined, both medically and spiritually, the physician and the priest working in close collaboration. The archbishops are asked to consult with the appropriate medical authorities with a view to setting up an advisory panel consisting of priests and physicians, and it is recommended that exorcism should be practiced only with the authority of the diocesan bishop after he has consulted with this advisory panel.

Radiotherapy in Carcinoma of the Lung.—In a series of 347 patients with inoperable bronchogenic carcinoma 200 were treated by radiotherapy. The results were analyzed by K. Sicher (*Practitioner* 180:695, 1958). Symptomatic relief was about the same, irrespective of the dosage used. About 70% of patients obtained excellent or good relief, but the percentage of objective improvements was higher among those treated with elaborate techniques and a larger dose, and these patients also had a better survival rate. Of 23 patients who survived a year or more, 16 received more than 4,000 r. The difference in survival time between treated and untreated patients was statistically significant: 11.5% of the former were alive after one year, compared with only 2% of the latter, and after three years 4.5% of the treated patients were still alive but none of the untreated. As most of the patients were in an advanced stage of the disease, a survival rate of 4.5% for three years is noteworthy. Those who survived longer after treatment also enjoyed symptomatic relief, and therefore their lives were really worth prolonging. The policy adopted in this department as a result of this survey is that every patient with an inoperable bronchogenic tumor be given the benefit of radiotherapy, unless the expectation of life is thought to be less than one month. Even in some of these unfortunate patients a short course of deep x-ray therapy is helpful if severe respiratory symptoms are present.

Ultrasonic Diagnosis.—The use of the echo patterns obtained by pulsed ultrasound in the diagnosis of large intra-abdominal masses, including the gravid uterus, pelvic tumors, and ascites, was investigated by Ian Donald and co-workers (*Lancet* 1:1188, 1958). Masses containing fluid were easily but crudely demonstrated. Their experience of 78 patients in whom diagnosis was quickly verified by laparotomy and subsequent histology indicated that ultrasonic diagnosis is still crude and that the preoperative diagnosis of histological structure is still far off. Their most interesting patient was one in whom the clinical diagnosis was convincingly that of a uterine fibroid, but ultrasonic scanning revealed a fetus in the uterus, and the diagnosis of pregnancy was subsequently confirmed. On the basis of experiments with newborn kittens, it was concluded that exposure of the kittens to more than 30 times the dose of ultrasound necessary in its diagnostic use produced no detectable neurological changes.

LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Sherman Anti-Trust Act: Practice of Medicine as Interstate Commerce.—This was an action for treble damages for violations of the Sherman Anti-Trust Act because of the allegedly wrongful refusal of the defendant society to admit the plaintiff as a member. From a judgment in favor of the defendant, the plaintiff appealed to the United States court of appeals for the eighth circuit.

The plaintiff was a licensed physician and surgeon and had been practicing his profession in Washington County, Arkansas, since 1935. He alleged that in the course of his practice he received, accepted, treated, and administered to patients from Arkansas, Oklahoma, Kansas, Missouri, Texas, and other states and that he would have had many more patients from those, and other, states if he had been permitted to become a member of the Washington County Medical Society. He had applied for membership four times but had been rejected each time, and he alleged that the defendants had combined and conspired among themselves not to admit him to membership in the society. This, he alleged, was a violation of the Sherman Anti-Trust Act.

The defendant contended that the Sherman Act was not applicable to the facts set forth in the plaintiff's complaint and that the court was therefore without jurisdiction to hear the case. It is to be noted, said the court of appeals, that the complaint is confined to the plaintiff's private medical practice. It charges no economic burden on the public by reason of the alleged acts of the defendants. There is no charge that the rejection of the plaintiff's application for membership in the Washington County Medical Society resulted in the raising or fixing of fees charged the public by other physicians. There is no allegation in the complaint remotely suggesting that the acts of the defendants cast any burden on interstate commerce. The mere fact that the plaintiff, at his location in Arkansas, may be treating patients from other states who must travel interstate does not result in his practicing his profession in interstate commerce, as the transportation of such patients is incidental. The practice of his profession, as disclosed by the allegations of his complaint, is neither trade nor commerce within Section 1 of the Sherman Anti-Trust Act. The plaintiff has not been prevented from practicing his profession, but in the final analysis his complaint is that he could practice it more profitably but for the acts of the defendants. The Sherman Anti-Trust Act was not primarily to protect the individual but to protect the general public economically, and a private party may not recover under the act unless there has been an injury to the general public economically.

The court of appeals pointed out that a prior decision had held that the practice of medicine, as conducted within the State of Oregon by doctors of Oregon, is not trade or commerce within the meaning of Section 1 of the Sherman Act. This was affirmed by the Supreme Court of the United States. In another case, the court held that the practice of the healing arts in Colorado is wholly local in character. "The mere fact," said the court in that case, "that a fortuitous and incidental effect of such conspiracy and acts may be to reduce the number of persons who will come from other states and countries to the Spears Hospital for chiropractic treatments does not create such a relation between interstate and foreign commerce and such local activities as to make them a part of such commerce."

In conclusion, the court of appeals said that the plaintiff's complaint is, in effect, that the practice of his profession would have been more profitable to him had the defendants not deprived him of membership in the Washington County Medical Society. The plaintiff was not prevented from practicing his profession, and the complaint is wholly lacking in allegations essential to a cause of action under the Sherman Anti-Trust Act. The judgment in favor of the defendants was therefore affirmed. *Rigall v. Washington County Medical Society, et al.,* 249 F(2) 266.

THE LEISURE CORNER

PLAYING HANDBALL

Handball requires a great deal of stamina, and for that reason many doctors enjoy batting around a rubber ball with a light leather glove. Handball is Irish in origin and a thousand years old. Robert Ripley, the "Believe It Or Not" man, who himself was an ardent enthusiast of the game, claimed that it was the oldest of all games played with a ball. Today, handball is played more often on this continent than anywhere else in the world. About 1850, William Baggs of Tipperary developed the first scientific method for playing the game. He made extensive tours in the United States, coaching and defeating all opponents. He originated new ways of striking the ball so that it would hop or stay close to the floor surface.

Although the rules governing the old and the new versions of handball are very much the same, two important factors, the ball and the court, are quite different. The old-time hard ball suggested a miniature baseball. It had a tight horse-hide covering and was sewn like a baseball, with a center of cork and tightly wound with strips of crude rubber and thread or yarn. The use of this type of hard ball required large, wide courts. Unlike the modern game, kicking was permitted and players were quite adept at returning particularly low balls with their feet.

The adoption and standardization of the soft ball game began during the 1890's when a new ball, about the size of our present day tennis ball, put in an appearance on handball courts in New York City. When players started to use this new type of soft ball, they found that it was not lively enough and that the game was too slow. However, what the soft ball innovation actually did accomplish was to popularize handball among men, boys, and girls. Hitting a ball against a brick wall of a building spread the popularity of the game from coast to coast.

All of this led to the downfall of the hard ball game. The change in the type of ball used produced a new method of playing handball. It was then called single-wall handball and was now strictly an American game. Its growth has been more rapid than the four-wall game chiefly for two reasons. First, playing facilities became more readily available, for it was now possible to play against any smooth surface. Secondly, it was possible to set up more adequate spectator accommodations by constructing bleachers on three sides of the court.

Many doctors are in need of some type of recreational physical activity. It is often advisable for them to have some form of exercise which is conducive to good health and provides mental relaxation. For the older man, handball is a wholesome and invigorating diversion that can be played leisurely without a great amount of effort. Coordination of all parts of the body is developed, and the desire for improving one's game always provides a challenge. There are few games which require so great an amount of scientific play, where quick choices are presented and split-second decisions have to be made. Any doctor can learn to play the game in a relatively short time and enjoy harvesting some of the physical benefits derived from a 45-minute workout. In fact, many players have found it is possible to obtain all the exercise they need in a shorter time. They usually play on indoor courts, and the weather does not alter their activity. The opportunity to use both hands in a like manner is another distinct advantage of handball over other games. This factor is particularly important, as it develops better all-round postural habits. Aside from the conditioning value of the game, is the need for coordination between eye and body movement that is exceedingly stimulating to anyone who plays. Handball is one of the least expensive of all the sports, as the initial outlay is the price of a pair of gloves and a ball. If necessary, any pair of old leather gloves can be used.

For the beginner it is better that he play by himself the first few times on the court, practicing each shot until he has mastered the fundamentals of play. For the first few times it is good practice to throw the ball so that it comes off the wall at different angles. As you continue to play you will learn to anticipate the position you have to take in order to make a good return shot; this saves many steps and results in a more scientific play. The person new at the game should concentrate on the underhand stroke, especially with his weaker hand. The ball should be played as low as possible in the beginning, with the player constantly attempting to be in position for the next shot.

It is interesting to note how a game of handball has the faculty to bring out both good and bad qualities of a person. Handball is usually played without the service of a referee, except perhaps in tournament play. There is an opportunity for blocking, shoving, and an occasional push. When these take place the activity loses its enjoyment, and the sport ceases to be a game of skill. It is therefore helpful to be fully aware of the few court procedures so that no embarrassing moments will alter the pleasure of the game.

For instance, do not cross in front of the ball, thereby obstructing your opponent's view, but allow him a fair opportunity to make his return shot. When playing on a warm day, try to keep the ball as free from perspiration as possible, since there is little pleasure in playing with a ball that slides along the wall in a different manner each time it strikes. If a play is questionable, it is customary to play the rally over. (A ball striking the front wall close to the floor is good if it comes out fairly straight. If it comes up, it has hit the floor first, hence, bad.) Should your opponent call a "hinder," it is usually good form to accept the decision without further consideration. The theory behind handball strategy is the same as that behind most sports, namely, placing the ball out of the reach of your opponent. After the rudiments of the game are mastered, and the player is able to devote his time and energy to out-guessing his opponent, the game picks up a thrill with every shot. The most common method of hitting the ball is with the hand in a semi-cupped position, with the fingers slightly close together. The ball strikes the cushion portion of the hand at the base of the fingers, but depending on the stroke of the arm, the ball may slide off between the thumb and forefinger.

At Columbia University, handball is a highly regarded game; it is included as one of the three recreational physical education activities required of every student. It is taught in small groups of from 10 to 25 students. Many colleges have a "sports library" for students interested in the game. An occasional demonstration by outstanding players throughout the course is of value to the novice player from the standpoint of motivating and learning. Many Y. M. C. A.'s have programs of instruction and playing, and these are available to busy doctors.

MISCELLANY

ELECTRONICS AND BIOLOGY

David Sarnoff, New York

Because of its amazing versatility, electronics has had an impact on virtually every aspect of human existence. That includes the field of health and healment, where electronics already has made some significant contributions and where its potentialities for the future seem even greater.

Kinship of Electronics and Biology

The more we explore their relationships, the more impressed we become by the kinship of electronics and biology. Both depend heavily on physics and chemistry and present phenomena which can be grasped only when the structure of the atoms, and the forces within and between them, are understood. Increasingly each of them depends on a close study of the solid, liquid, and gaseous states of matter.

But the kinship goes much deeper. Perhaps the most significant clue to their affinity is that electronics and biology alike place basic emphasis upon minute component elements, the so-called elementary particles.

In the past, man concentrated attention on massive entities and their gross or general form. In the electrical field, the primary concern was with big motors and generators, large conductors, and the like. In biology, interest was directed to the visible and tangible parts of the living organism. Structure held the center of the stage.

But, in recent years, we have seen a radical shift of emphasis to the tiniest particles—the invisible building blocks of the universe. The infinitesimal has been recognized as the most potent and controlling aspect of nature. We in electronics work with the atom and its nucleus, with electrons, protons, neutrons, ions. You in biology study bacteria, viruses, the gene, the cell, and the still smaller building blocks—the complex molecules of biochemistry.

That meaningful parallel is reflected in the guiding principles, methods and insights, trends and scope of inquiry which are common to both fields. What is more, as our tools of investigation are further sharpened, the present strong resemblances portend discoveries which may reveal actual identity.

Man as a Communication System

Another analogy, one that I find endlessly fascinating, is packed with rich promise for both our sciences. I refer to the fact that communication theory (which is at the heart of many electronic systems) applies also to human beings. The degree of similarity is really astonishing.

About 70 years ago, a French physicist, Edouard Branly, was testing different theories as to how nerves carry messages from the skin to the brain and back again. He noted that the nerves are not continuous fibers but are formed of neurons and synapses, closely massed but not necessarily in contact. Applying this discovery to electromagnetic or radio waves, he found to his own amazement that a similar principle held good. The first successful detector of radio waves, the Branly detector, was thus the result of observations in the biological area.

Branly's intuition was merely a beginning. Since then it has been demonstrated that the physiological message-carrying system is the archetype of what the electronic engineer seeks to duplicate.

In order to form an integrated functioning unit, man's trillions of cells must be electrically and electrochemically interconnected. This "intercom" system consists of groups that operate concurrently in what we in electronics call a "multiplex system." The connective channels, or neurons and secretions, work both inwardly and outwardly. Inwardly, they carry impressions from the sense organ to corresponding cells within the central nervous system in the brain and spinal cord. Outwardly, they con-

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Chairman of the Board, Radio Corporation of America.

Read before the World Congress of Gastroenterology, Washington, D. C., May 25, 1958.

trol muscles, glands, and other body elements. They function to coordinate messages from one part of the body to another. Additional channels continually report back to the brain the extent to which a willed act is being performed, and associated brain cells initiate and control any needed corrective action. In electronics, this is the familiar principle of "feedback."

This marvelous communication system inside man makes the most elaborate outside communication system elementary by comparison. Yet the underlying parallels between the body's communication system and that of electronic equipment—in the most advanced computer or "electronic brain," for instance—are remarkable. They challenge our imagination.

Contributions of Electronics to Biology

Already the impact of electronics upon biology, medicine, and related disciplines is far greater than many practitioners, let alone the public, realize. A great array of electronic tools and techniques is today in use or available for use by physician and surgeon, anesthetist, and radiologist. And even more promising devices are now in various stages of gestation in electronic laboratories.

Literally every electronic advance for communication or industry yields new knowledge, enabling readier access to hitherto impenetrable recesses and aspects of the human body and the production of more effective instrumentalities for medical and surgical practice.

Television, for instance, is thought of primarily as a mass medium of information and entertainment. Yet closed-circuit TV, both in black-and-white and in color, is becoming a vital adjunct to medical education. Electronic computers, to cite another instance, are thought of primarily in relation to industry and business. Yet their capabilities are multiplying the effectiveness of every man and woman engaged in biological and medical research.

The researcher in biology and the diagnostician in medicine depend largely upon the tools at their disposal. They need electromechanical, electrochemical, and electrothermal equipment; acoustic devices; high-speed apparatus for measuring, recording, and analyzing data; methods of high magnification.

In all these respects, electronics is increasingly at their service. It can relieve the professional worker from many routine tasks by collecting and processing information automatically, instantaneously, and with unprecedented accuracy. Electronic devices can perform jobs involving differentiation between similar objects. They can count them in a given area, record and store the resulting data, make them instantly available when needed, and compute the degrees of their correspondence or difference.

One of the major contributions of electronics is by this time fairly familiar: the electron microscope, which surpasses the capacity of the optical microscope at least 100-fold. Of immense importance in chemistry, metallurgy, and other industrial fields, it is equally if not more valuable to the biological and medical worker.

Then there is the electronic stethoscope, which picks up heart sounds, chest vibrations, or sounds from other organs and amplifies them accurately for a telephone headset or loud-speaker. It yields far more information than the conventional stethoscope. Recently a capacitance pick-up has been developed for the study of heart sounds and the early detection of heart defects.

Today blood pressure and spinal fluid pressure can be measured electronically and indicated directly. The same is true with respect to currents generated within the brain. New electronic tools promise significant expansion and refinement of present methods of electroencephalography.

At the research end, the so-called alpha and other rhythms in brain-generated electricity have been studied for as many as 50,000 samples obtained and recorded in three minutes, then promptly analyzed by electronic means. Unquestionably, electronic techniques can be expected to yield an enormous new understanding of the brain, ultimately helping to solve some types of mental disorders and some brain tumor problems.

Similarly the principles of radar and sonar, so vital to national security, have found valuable applications in diagnostic medicine. Sonic and ultrasonic vibrations are focused on the bodily area under examination. When they strike internal structures, they are absorbed or reflected. The reflections are systematically detected and the location of an obstruction exactly charted. Unlike x-rays, ultrasonic beams can detect cysts and growths which differ in structure, but not necessarily in density or effective atomic weight, from the surrounding mass.

Electronics is of increasing importance, also, to the radiologist. He has always contended with the risks of physiological damage where prolonged exposure is necessary. One solution of this problem has been found in electronic methods of amplifying the brightness of the picture, thereby permitting a smaller x-ray dosage. It is also proving possible electronically to sharpen the edges and the contrast in x-ray pictures and to improve stereoscopic pictures, those taken from a number of viewing angles simultaneously.

Electronics also permits the direct study of organic specimens with another kind of invisible radiation, the ultraviolet. While unstained cells are commonly uniformly transparent in the visible, their component parts exhibit sharply differentiated absorptions in the ultraviolet spectrum. The newly developed ultraviolet color-translating television microscope employs a modified color television technique to translate differences in ultraviolet absorption into visible color differences. With its aid, natural tissues yield color pictures revealing at a glance the distribution of important chemical constituents in the cell. The great promise of the method for fundamental biological research is obvious.

Dr. Vladimir Zworykin and his colleagues recently have produced a startling instrument that has come to be called a radio pill—a miniscule radio transmitter which can actually be swallowed. Because the frequency of its signals is governed by the variations of pressures on the capsule, a receiver outside the body gathers telltale information from inside the stomach.

Without doubt this boldly conceived device represents a breakthrough in biological research and diagnostics, since it is the forerunner of a multitude of coming adaptations. They should enable us to study various conditions in the body with a minimum of surgery and, in some cases, without recourse to surgery. At other times they will provide the diagnostic data that, when surgery is indicated, will make it more accurate.

Artificial Bodily Organs

The surgeon, in fact, has a particularly large stake in enlisting the electron in his service. The most spectacular development in this area is electronic mechanisms acting as temporary substitute organs in the human body while the natural organ is being worked upon. That a man-made device could ever, however briefly, take over the functions of a bodily organ would have seemed wildly improbable before the electronic age. But to a limited extent this goal has already been reached, bringing within the bounds of feasible surgery some operations formerly considered imprudent, if not impossible.

The most dramatic of the substitute organs is the artificial heart. Here we have an electrically driven and electronically controlled device which bypasses blood flow around the heart and carries out the normal effects of the heart beat while maintaining a pace adjusted to the needs of the patient. When one reflects that the blood must not clot within the artificial heart, that temperatures and pressures must be maintained with the utmost precision, it is clear that here we have a case where medical science is stranger than science-fiction.

Paralleling the artificial heart, we have the development of an artificial lung and an artificial kidney, each bypassing the natural organ while it is being examined or repaired, each made possible by electronic sensing and control devices.

Inevitably one wonders whether the use of these artificial organs need forever be restricted to the operating room. In theory, at least, it is conceivable that one day compact electronic substitutes will be provided on a permanent basis to replace organs that have become defective through injury or age.

Artificial kidneys, lungs, and even hearts may then become as familiar as artificial teeth or hearing aids. Indeed, one may imagine a man walking around in apparent good health with several of his organs replaced by the refined electronic substitutes of the future. Admittedly the idea is fantastic, but, as the marvels of electronics unfold, the line between fantasy and fact is ever harder to define.

In the field of orthopedics, electronic methods are not yet at the point of major utility but important possibilities are in evidence. Electronic apparatus for systematic and automatic exercise of any part of the body—in cases of partial paralysis, for instance—are already far advanced.

More important, electronics promises sensational improvement of prosthetic devices. At the heart of this promise is the electronic capacity to amplify the minutest muscular efforts and impulses to almost any desired magnitude. The outlook—though as yet only a hope—is for equipment which, attached to the stumps of an amputated limb or to some other part of the anatomy, will actuate and control movements of an artificial leg, arm, or even fingers with acceptable precision.

For the nearly deaf, the bone-conduction receivers or compact electronic equipment for large audio amplification now in use are being constantly improved, and other expedients under study show encouraging prospects.

Among the most humanly exciting potentials now at the experimental stage are devices that in some measure "see" for the blind. Interesting beginnings have been made, for example, toward electronic detection of obstacles in the path of the blind or sudden changes in the ground or pavement levels. Progress is being registered, too, in electronic equipment for translating ordinary type into audible signals, thus enabling the blind to "read" conventional printed matter.

This inventory of the electronic contribution to biology, medicine, and surgery is far from complete, of course. Every piece of new equipment, it should be remembered, tends to become the progenitor of a whole family of devices, each adapted to additional uses as it is refined to meet more complex conditions.

The same principles of energy under precise controls which, at one extreme, guide a man-made satellite into an orbit around our planet are applied, at the other extreme, to arm the biological professions with unprecedented instrumentalities for the pursuit of their specialized knowledge and the healment of human beings.

Color Television and Biology

Anything that the human eye can see can be transmitted by television in true color. This truth has endless implications for everyone directly or indirectly engaged in the alleviation of bodily suffering. The horizons opened up are so wide that I need only mention a few to suggest their magnitude.

The details of an operation or the appearance of a lesion can now be sent to any desired point for examination. Any malfunctioning area can be studied without the examiner actually visiting the patient. We can envisage a time when the individual patient, in a hospital or at home, can be viewed and advised by a physician from any distance. Microscopic slides and x-ray pictures can be studied at places remote from their physical location. Any picture in motion—let us say of an operation in progress—can be viewed directly, in normal size or greatly enlarged, at any desired point of reception.

Panels of specialists hundreds or thousands of miles apart can consult about a case. Fully illustrated symposiums can be held in many hospitals or meeting halls in widely scattered cities at the same time.

The living record of an operation or of the history of a medical case, moreover, can be put on magnetic color tape for leisurely viewing and study in the future. In the hospital, a skilled supervisor at a central control station can literally "see" the entire institution without moving from his seat, dispatching nurses and doctors to points where they are needed.

Many of you are aware that the nation's first assembly of closed-circuit compatible color television for hospitals and research laboratories has been installed by the Radio Corporation of America at the Walter Reed Army Medical Center in Washington, D. C. It interconnects the Armed Forces Institute of Pathology, the Army Institute of Research, and the Walter Reed Army Hospital. The benefits in efficiency, coordination, saving of time, saving of manpower, and other respects, I am told, are already impressive.

The same instrumentality, closed-circuit TV, is finding more and more employment in education. Groups and individuals all over the country can hear and view illustrated lectures simultaneously. This makes possible not only specialized instruction for medical and nursing students but more convenient and more economical postgraduate courses for interns and refresher courses for practicing physicians.

It means that vital information and skills in one community have become readily available to the rest of the country. It means that the genius of an outstanding teacher or specialist, hitherto confined to one university or hospital, can be made accessible to interested men and women anywhere. In a period when significant new medical knowledge and techniques are constantly being unfolded, this electronic ability to disseminate them widely and rapidly should prove of inestimable value.

Electronic Computers for Biological Studies

Equally important is the ever-expanding contribution of electronic computers to biological, medical, and related sciences. Every physician, every researcher, every hospital struggles with the burden of rapidly accumulating data requiring classification, analysis, storage for instant availability for reference or study. An ever-larger share of that burden is being assumed by modern electronic data-processing equipment, with tremendous economies in time and gains in precision. Electronic performance provides almost instantaneously the kind of statistical and probability findings which would, by conventional methods, have required days or weeks of tedious work.

This element of time-saving is more important than might appear at first glance. In all areas of research, what is called the lead-time gap—the interval between the discovery of a basic principle and its practical application—is unduly long. But in biological work the gap is particularly protracted, owing to the extreme complexity of biological systems and the great caution essential when human health and life are at stake.

This is where the electronic worker comes increasingly to the assistance of the biologist. To begin with, speedy communication makes available to each experimenter the new knowledge of others in the field. Often needless duplication of effort is thus avoided and the pieces of an emerging puzzle are more swiftly fitted together. Beyond that, automatic analysis of masses of data sharply telescopes the time ingredient.

Consider, for example, the complexity of the action of the endocrine glands. We know broadly that certain mechanisms control hormonal secretions, the effects of these hormones, and their elaborate interactions. Definitive conclusions, however, have been hampered by lack of sufficient data, speedily and accurately analyzed and reduced to dependable statistical forms. The enlistment of electronic "brains" in the enterprise obviously should shorten and sharpen the processes of inquiry.

Now that we have learned how to split the atom and how to reconstitute new atoms from old ones, or from energy itself, perhaps it is not too much to hope that the combined efforts, knowledge, and skills of biologists and electronic scientists may lead to a deeper understanding of the human cell and to the discovery of means for modifying its structure and its functions. Once this is achieved, we may find the answer to such dread diseases as cancer.

Electronics and Biology—Sister Sciences

Viewed from this broad perspective, we can say that the youngest of sciences, electronics, and one of the oldest, biology, are converging sciences. The very complexity of man's structure and its electrochemical aspects points up the natural relationship between them.

Electronic devices have the extreme sensitivity the biologist needs when delicate structures or tenuous phenomena must be examined. They can probe deeply and delicately and provide high magnification of what the apparatus finds. Only electronics is able to deal with the ever-increasing volume of data of biological structure and function.

Of course, it is dangerous to push affinities and analogies to excess. We must never forget that the stuff of life transcends, in its complexity, the most ambitious inventions man can imagine, let alone construct. Even the most elaborate man-made apparatus is primitive when matched against a living creature. The largest electronic computer, for example, may have one million storage elements, whereas the human brain has perhaps a hundred billion cells.

In any scientific endeavor, humility rather than pride is nourished by progress. For we realize that the more we learn, the more remains to be learned. Even in its most spectacular achievements, science can imitate but can never surpass the marvels of the Divine order.

It was by watching the effortless soaring of birds in the skies that Leonardo da Vinci and experimenters after him were emboldened to attack the problem of heavier-than-air flight. Radar is but a partial replica of the mechanisms whereby a bat finds its way in darkness past obstacles. The electronic submarine navigational equipment called sonar does not approach in perfection the means by which fish guide themselves under water. Man, in the final analysis, invents nothing that is more than a pale shadow of nature, from which he draws his inspiration and his material.

Yet the new science of cybernetics has shown that somewhat similar controls, feedbacks, and methods of operation prevail in man's electronic handiwork and in man himself. It is too early to judge the ultimate meaning and utility of these affinities. It is premature, too, to speculate in any detail on what the skilled electronic designer may accomplish in the future. Suffice for our time that electronics and biology are now treading a common path of inquiry, thrilling in its possibilities.

I have the utmost enthusiasm concerning the prospects of biology and electronics in their collaboration for the service of mankind. I am convinced that their relationship, already so close, is destined to become closer and more fruitful with every passing year.

The time may well come when science shall have fully uncovered the nature and functioning of both the energy-packed atom and its combinations on the one hand, the living cell and its aggregations on the other. At that point knowledge of the nature of life itself—the ultimate unity under the appearances of infinite diversity—may be revealed to us.

We in the electronics field believe that our labors will expand and enrich yours. At the same time we know that we shall continue to learn much that is helpful to electronics from your victories in the biological realms.

This rough sketch of some of the roads at which electronics and biology meet, is necessarily incomplete. However, I hope it may serve further to stimulate the curiosity and intensify the interest of scientists, researchers, and practitioners in both these fields. Their combined efforts, I feel certain, will lead to new discoveries and devices that will advance the health and welfare of all mankind.

30 Rockefeller Plaza (20).

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Concept of Early Diagnosis in Strokes. R. G. Siekert and C. H. Millikan. A.M.A. Arch. Int. Med. 101:872-880 (May) 1958 [Chicago].

Focal cerebral ischemia or infarction (commonly referred to as thrombosis) accounts for some 80% of all strokes. In the absence of specific measures for the prevention of cerebral atherosclerosis, attention need be drawn to means that can be utilized to anticipate and thereby possibly prevent the occurrence of selected varieties of strokes. Three syndromes are delineated: the syndrome of intermittent insufficiency of the vertebral-basilar arterial system; the syndrome of thrombosis within the basilar arterial system; and the syndrome of intermittent insufficiency of the internal carotid arterial system. Illustrating case histories are presented with each of these 3 syndromes. The syndrome of intermittent insufficiency of the vertebral-basilar arterial system consists of sharply episodic attacks of visual dimness, weakness of the limbs (monoparesis, hemiparesis, quadriparesis), dysarthria, dysphagia, diplopia, confusion, and vertigo in various combinations. Between attacks the patient is well. During an attack, neurological abnormalities are present. A single episode may suggest the diagnosis if it includes most or all of these symptoms. Usually, however, a single episode is a fragment of the whole, and one can only suspect the diagnosis. It is when a group of these episodes occurs over weeks or months with the inclusion of most of the above-mentioned symptoms that one can be more certain of the diagnosis. Careful study need be made to determine that intermittent vascular insufficiency is the fundamental factor involved, rather than some other cause, such as an expanding intracranial mass or epilepsy.

The neurological signs noted in the second syndrome when thrombosis with the basilar artery is in the process of occurring or has actually occurred include the following: weakness of the limbs, often with extensor spasms; pseudobulbar or bulbar weakness in the form of dysarthria and dysphagia with a weakened pharynx and palate and slowness and decreased protrusion of the tongue; ocular abnormalities, particularly in the pupils, where inequality, miosis, and nonreaction may be seen, or in the extraocular muscles, which are weakened in various combinations; homonymous hemianopsia, which may be bilateral; and facial weakness, either "central" or "peripheral" in type. The last, with contralateral hemiparesis, usually indicates involvement of the brain stem. Hyperpyrexia is common.

The syndrome of intermittent insufficiency of the internal carotid arterial system consists of attacks of unilateral impairment of motor or sensory function or both. With involvement of the artery to the dominant hemisphere, aphasic disorders may be seen. Decrease in vision or blindness in only 1 eye (amaurosis fugax), and that on the side of the involved artery, will be seen in some instances. While the degree of involvement will vary, the complexity is not as great as in vertebral-basilar insufficiency. Here, too, a single attack may in no way be diagnostic, but a group of attacks may permit one to make the diagnosis. With early recognition of these types of cerebrovascular disease, treatment may be instituted prior to the possible occurrence of extensive cerebral infarction. Treatment with anticoagulant drugs may prevent the continuation of these ischemic attacks and, therefore, also the possible occurrence of a catastrophic infarction.

The Fate of the Patients with Persistent Cavitation and Noninfectious Sputum ("Open-Negative") After Discharge from the Hospital. R. F. Corpe and F. A. Blalock. Am. Rev. Tuberc. 77:764-777 (May) 1958 [New York].

This report presents the preliminary experience of the authors with so-called "open healing" of tuberculosis cavities and with patients who have acquired a noninfectious status despite persistent cavitation under drug therapy. Between July 1, 1953, and Dec. 31, 1956, 159 patients with cavitary disease, sputum negative for tubercle bacilli, and pulmonary lesions stable on roentgenography were discharged from Battey State Hospital, Rome, Ga., and continued on drug therapy. On the basis of follow-up studies on these patients, the authors reached the following conclusions: It is safe to dis-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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charge patients with the "open-negative" syndrome to their home environment without creating a public health problem. The mortality rate in this group of patients was 3.8%, but these deaths occurred in patients who had not had bacteriological or roentgenologic relapse. They were not treatment failures. The reactivation rate was 8.8%. There were no additional reported bouts of suppuration or hemorrhage. There has been no discernible difference, up to the present time, in the reactivation rate between the Negro and the white race. The male sex has not fared as well as the female sex, 13 of the 14 reactivations occurring in men.

Only 2% of the patients were confined to their homes because of their physical disabilities. If such people can be adequately cared for in a home situation, they are much happier, and it is cheaper to maintain them on drugs outside the hospital than as inpatients. A considerable number of these people, even with cavitary disease, if given the opportunity, with public health clearance as to noninfectiousness, can become self-supporting and again take their place in society. Forty-five per cent of the patients had unlimited activity, and more than 25% were found to be working full time. The authors feel that these observations somewhat counterbalance their earlier belief that these cavities should be removed surgically or collapsed by thoracoplasty prior to the time when the patients could hope to return to their families and earn a living. Long-term follow-up observations on patients in this category are of extreme importance, since there are many unanswered questions, such as: How long should a patient with the "open-negative" syndrome be continued on drug therapy? This must be individualized, but a considerable number of these people should be continued on drug therapy indefinitely. On the other hand, among the group of 38 patients whose drug therapy had been stopped, there have been no reactivations to date.

Heart Failure of the Hunchback. T. Hanley, M. M. Plattis, M. Clifton and T. L. Morris. Quart. J. Med. 27:155-171 (April) 1958 [Oxford, England].

This paper deals with 24 persons with severe hunchback. Ten of these patients had severe kyphoscoliosis and heart failure. The clinical features, arterial blood-gas values, and pulmonary function of these 10 patients were compared with those obtained in the 14 persons who had severe spinal curvature but had not suffered from heart failure. It was found that severe kyphoscoliosis may reduce the total lung capacity and the vital capacity to as little as one-quarter of normal. The diminutive lungs are, however, ventilated with an efficiency only a little less than normal, and emphysema is usually slight. The diagnosis of kyphoscoliotic heart disease did not present great difficulty. In kyphoscoliotic heart failure peripheral vascular signs were predominant, and the clinical picture closely resembled that of anoxic cor pulmonale due to emphysema.

Reduced arterial oxygen saturation and retention of carbon dioxide were found in 8 of the 9 patients with true kyphoscoliotic heart disease, but these changes were present in only 2 of the 14 patients without heart failure. It was not possible to make such a clear distinction, simply by measuring either the volumes of the various compartments of the lungs or the efficiency of ventilation, between those with and those without a history of heart failure. Cardiac catheterization was done in 3 patients; it showed a moderate rise of the pulmonary artery blood pressure in 2 anoxic patients who had recovered from heart failure and a small rise in 1 patient who had not had heart failure.

Clinical and Microbiological Aspects of Salmonellosis. G. M. Eisenberg, L. Brodsky, W. Weiss and H. F. Flippin. Am. J. M. Sc. 235:497-509 (May) 1958 [Philadelphia].

In a previous report on 95 patients with salmonellosis seen during 1947-1952 at the Philadelphia General Hospital, it was pointed out that diagnosis on clinical grounds alone was frequently hazardous in view of the protean nature of the clinical manifestations. The practical importance of employing diagnostic antigens capable of demonstrating serum antibodies resulting from infections induced by Salmonella organisms, other than the classical typhoid-paratyphoid strains, was illustrated. Information on an additional 75 cases of bacteriologically proved Salmonella infections during the period from January, 1953, to June, 1957, was obtained subsequently from a review of records at the same institution, and it is these data which form the subject matter of the present report. The current study includes results of antibiotic susceptibility tests on cultures of the various Salmonella serotypes. Of the 75 patients comprising the study group, 40 were adults and 35 were infants and children.

Fever and diarrhea were encountered most frequently in both pediatric and adult patients, diarrhea being more common in the former. The proportion of patients with fever and the occurrence of vomiting was about the same in both groups. The over-all mortality rate was 20%; however, if the estimation of mortality is based only on those cases in which death was unquestionably attributable to the salmonellosis, the fatality rate is reduced to 5.3%. Fatalities occurred among infants and older debilitated individuals. In contrast to the experience in the 1947-1952 series, in which most of the deaths were associated with infection by Salmonella organisms of serogroup C, mortality in the present study was associated with strains belonging to serogroup B. Evidence is presented to support the view that any of the several clinical syndromes may be produced by the same or different Salmonella serotypes. The length of time that these organisms continue to be shed in the stools after apparent clinical cure of the patient is variable. Where such information could be obtained, this interval has ranged from 10 to 604 days, with an average of 127 days. In vitro antibiotic susceptibility testing of the 62 salmonellas isolated from patients revealed them to be uniformly sensitive to chloramphenicol. About one-half of the strains were susceptible to the tetracyclines, streptomycin being quite ineffective. No relationship between serotype and antibiotic susceptibility could be detected. Despite the in vitro superiority of chloramphenicol, its clinical use, either alone or concomitantly with other agents, exerted little, if any, influence upon the fatality rate.

The Treatment of Eosinophilic Lung (Tropical Eosinophilia) with Diethylcarbamazine. T. J. Danaraj. Quart. J. Med. 27:243-263 (April) 1958 [Oxford, England].

Earlier the author had demonstrated the efficacy of organic arsenicals in eosinophilic lung. The use of organic arsenicals, however, is associated with definite risks, so that a search was made for some form of treatment as effective but not toxic. Groups of patients were treated with various drugs—sulfathiazole, bismuth, penicillin, Achromycin, cortisone, piperazine citrate, and diethylcarbamazine—but only diethylcarbamazine was found to be of value. As diethylcarbamazine is known to be effective in the treatment of filariasis, it was important to exclude this disease. There was no evidence suggestive of past or present filarial infection in any of the 110 patients analyzed in this report. The duration of illness when they were first seen was variable, the shortest period being 1 week, and the longest 4 years; in the majority of the patients (97) it was under 6 months. The initial complaint was cough, which was most frequent and severe at night, occurring in paroxysms of a few minutes and productive of slight mucoid or mucopurulent sputum, which was sometimes streaked with blood; sleep was badly disturbed. A feeling of suffocation and breathlessness was usually present after each bout of coughing, and at times was severe enough to resembled bronchial asthma. The severity of symptoms was considered to be slight (cough only) in 9 patients, moderately severe (cough with breathlessness) in 75, severe (bronchial spasm) in 25, and very severe (status asthmaticus) in 1 patient. Occasional bouts of low fever, lasting for a few days, were noted in 24 cases. No history of allergy was obtainable, except in 1 patient, who suffered from attacks of urticaria. A family history of bronchial asthma was given by 6 patients. Abnormal physical signs, which were confined to the chest, were present in 88 patients and consisted of coarse crepitations and rhonchi heard over the bases of the lungs, together with bronchial spasm in 26 patients. In nearly all the patients radiologic examination of the chest revealed increased striations, with varying degrees of mottling.

The dosage of diethylcarbamazine given initially to 46 patients was that generally recommended in the treatment of ascariasis: 4 mg. per kilogram of body weight given 3 times daily for 4 days. Later, 2 larger dosages were tried: 6 mg. and 10 mg. per kilogram of body weight given thrice daily for 5 days to groups of 57 and 7 patients respectively. The average total adult dose for each of the 3 dosage schedules was 3,200 mg., 6,000 mg., and 10,000 mg. respectively. The drug was given after meals in the form of 50-mg. tablets, the sirup being used for children. Except for 11 patients who exhibited severe bronchial spasm and were treated with antispasmodics as well, the patients were given only diethylcarbamazine. The drug proved to be safe and effective in the 110 patients with eosinophilic lung. It had no effect on patients suffering from other diseases with eosinophilia. The results obtained compared favorably with those obtained with organic arsenicals. Diethylcarbamazine should replace the organic arsenicals, because the latter sometimes result in encephalopathy and death in a disease which, although incapacitating, has no mortality in itself.

Hypogammaglobulinaemia and Tuberculosis: Implications of Their Association, and Other Observations. R. Parkes. Brit. M. J. 1:973-976 (April 26) 1958 [London].

The author reports on a 22-year-old unmarried woman who from the age of 4 years had recurrent colds and from the age of 5 years had typical grand mal epilepsy. Pulmonary tuberculosis occurred at the age of 19 years, for which the patient was treated with streptomycin and isoniazid. The tuberculous upper-lobe consolidation in the right lung, which was present on admission to hospital, resolved over a period of 6 months. Bronchograms obtained 2 years after the institution of the antimicrobial therapy showed moderately severe "saccular" bronchiectasis of the anterior and apical segment of the upper lobe of the right lung. Otherwise the bronchial tree appeared entirely normal. Two years after tuberculosis was detected, acquired hypogammaglobulinemia was diagnosed on the basis of the history of continued bacterial infection, gamma-globulin deficiency on paper electrophoresis, zinc sulfate turbidity test, fractional precipitation, and absence of isohemagglutinins. Gamma-globulin replacement therapy was instituted with 0.5 Gm. per kilogram of body weight in 1 week as a loading dose, followed by 0.025 Gm.

per kilogram of body weight per week for 4 months. The patient was given 0.5 Gm. of gamma-globulin per kilogram of body weight per week for an additional 4-month period. She also was given methoin and phenobarbital in small daily doses as anticonvulsants. After 6 months' replacement of gamma-globulin, its serum level had increased more than threefold. Fewer grand mal seizures occurred, and petit mal attacks were rarely observed. Electroencephalograms were impressively better. Despite this striking improvement, there was no apparent connection between hypogammaglobulinemia and epilepsy. The patient was animated and cheerful, when previously she had been dull and lethargic. Respiratory infections and frequent inexplicable low-grade fever no longer occurred.

The patient's history suggested the presence of hypogammaglobulinemia 5 years at least before pulmonary tuberculosis developed, and tuberculosis was known to have been present for 2 years before gamma-globulin therapy was instituted. The association of hypogammaglobulinemia and tuberculosis is probably coincidental, and they bear no cause-and-effect relationship to one another. The natural course of tuberculous disease appears to be unaffected by hypogammaglobulinemia. Both delayed hypersensitivity and serum antibody response to tuberculosis appear to function normally in patients with hypogammaglobulinemia, so that in normal persons the 2 phenomena may be independent of gamma-globulin and may be to a large extent related to a cell mechanism (leukocytes and other body cells), although the possibility of an unidentified serum protein fraction sharing such immunological powers is not excluded.

Hypertension and Diabetes Mellitus. P. Freedman, R. Moulton and A. G. Spencer. Quart. J. Med. 27:293-305 (April) 1948 [Oxford, England].

The blood pressure was measured in 1,100 patients attending a diabetic clinic, and the data were analyzed in terms of the incidence of hypertension in each age and sex group. Hypertension was common in both sexes, and the incidence steadily increased with age to a maximum of 92% of the female and 81% of the male diabetics at 70 to 79 years. A strong clinical impression was gained that hypertension was more common in diabetics than in a general hospital population. Statistical analysis, however, clearly showed that this difference is largely a false impression due to the abnormal age and sex distribution of the diabetic population. From 10 to 69 years of age, in both sexes, there was no significant difference in the incidence of hypertension in diabetics as compared with a nondiabetic population. It was only at 70 to 79 years that high blood pressure was distinctly more common in diabetics.

Severe hypertension (diastolic pressure over 125 mm. Hg) is rare in diabetes, the incidence being 0.5% in the male and 1.4% in the female subjects, which is less than in a general hospital population. Advanced hypertensive retinopathy, excluding diabetic retinopathies, was not seen in any of the diabetic subjects, except in those with pheochromocytoma. Data are given on the apparent incidence of hypertension due to various renal and endocrine disorders in diabetes. Diabetic nephropathies were diagnosed in 27.5% of the patients whose diastolic blood pressure was over 100 mm. Hg. The arm circumference was measured in all the hypertensive diabetic subjects and was found to be an important factor in determining the level of the blood pressure in 26.5% of these patients.

SURGERY

Acute and Chronic Thrombosis of the Mesenteric Arteries Associated with Malabsorption: A Report of Two Cases Successfully Treated by Thromboendarterectomy. R. S. Shaw and E. P. Maynard. New England J. Med. 258:874-878 (May 1) 1958 [Boston].

The authors report on 2 men, aged 54 and 58 years, respectively, with occlusion of the superior mesenteric artery resulting in intestinal ischemia associated with malabsorption. The first patient had been admitted to hospital because of progressive bilateral intermittent claudication. Aortography showed a narrowed aortic bifurcation and complete occlusion of the right external iliac artery. The patient was operated on, and an aortic homograft was sutured end-to-side to the abdominal aorta, the right limb of the graft being anastomosed end-to-side to the common femoral artery and the left to the popliteal artery. On the third postoperative day the patient had abdominal cramps and passed a liquid stool containing occult blood. The abdomen remained nontender until the 16th postoperative day, when suddenly severe generalized abdominal pain occurred and peristalsis disappeared. At reexploration 9 hours later the entire small and large intestines from the ligament of Treitz through the midsigmoid appeared pale and cyanotic. There were no pulsations in the celiac axis, in any of its 3 major branches, or in the superior mesenteric artery and its branches. A pancreatic necrosis was observed, which appeared to be of at least 1 week's duration. The superior mesenteric artery was opened through a longitudinal incision and was found to be occluded by a brownish thrombus and atheroma in its proximal 2 cm. A proximal thromboendarterectomy was performed through this arteriotomy with resultant excellent flow from the aorta. An amazing recovery of the small intestine resulted, while the large intestine remained cyanotic. A loop transverse colostomy was performed, so that the circulation of the colon could be observed in the postoperative period. Localized signs of peritonitis developed on the second day, and exploration was again carried out. The colon remaining within the abdomen was obviously viable, although there were 2 or 3 small necrotic areas in the wall of the defunctioned transverse colon. These were surgically patched with tabs of fat. The appendix was necrotic, and appendectomy was performed. Colostomy diarrhea and abundant drainage from the wounds, with the occasional casting out of a piece of pancreatic slough, continued for several weeks. The stools were found to contain increased amounts of fat. One month after the operation studies of intestinal absorption were performed, which showed a considerable defect in the absorption of fat, sugars, and vitamin B_{12}, with improvement during the 4-week period of observation. The patient was discharged 2 months after the thromboendarterectomy; he gained weight, was free from gastrointestinal symptoms on an unrestricted diet, and resumed full-time work.

These observations suggested that atherosclerotic occlusive disease in the arteries of the abdominal viscera may behave as it does in the brain, heart, and extremities, progressing more rapidly than collateral circulatory development and producing a picture of malabsorption, intermittent abdominal gain, and weight loss terminating in acute intestinal infarction. This was the sequence of events which occurred in the second patient in whom absorption studies were performed before and after the surgical correction of chronic intestinal ischemia and in whom the diagnosis was established preoperatively by aortography. Although major arterial branches to the abdominal viscera other than the superior mesenteric artery were involved with occlusive disease, restoration of continuity in the superior mesenteric artery alone was sufficient to provide symptomatic relief of ischemia. Since the absorptive functions of the intestine may be assumed to be dependent on its blood supply, it is not surprising that impairment of this supply should be accompanied by malabsorption. The diagnosis should be considered in certain patients with unexplained malabsorptive states, and thromboendarterectomy may represent an effective therapy in these patients, as well as in those in whom mesenteric vascular thrombosis results in intestinal infarction.

Lung Resection in Tuberculosis. I. S. Kolesnikov. Vestnik. khir. 80:3-10 (March) 1957 (In Russian) [Leningrad].

Kolesnikov reports on 1,000 pulmonary resections performed for pulmonary tuberculosis in Leningrad during the past 5 years. The indications for elective resections were strict. The majority of the patients operated on had far advanced fibrocavernous tuberculosis. The sputums of all the patients were positive for tubercle bacilli. The patients selected for resection were those that showed no improvement from other methods, including collapse therapy. Pneumonectomy was performed on 23.3%, bilateral lobectomy on 4.6%, lobectomy on 30.6%, segmental resection on 28%, and various other types of resections on 13.5%. Endotracheal potentiated ether-oxygen anesthesia was used in 950 cases. Fifty patients were operated on under local anesthesia. The author stresses the desirability of resecting as little as possible of the lung. He does not rule out the employment of pulmonary collapse and of cavernostomy, each of these operations having its own indications. A closer contact between surgeons and internists should bring about earlier transference of patients to the surgeon and in that way should diminish the number of mutilating operations, such as pneumonectomy and bilateral lobectomy, and at the same time should increase the number of segmental resections.

Segmental Occlusion of the Femoral Artery and Femoral and Popliteal Aneurysms: Surgical Aspects. D. A. Felder and T. O. Murphy. Minnesota Med. 41:322-326 (May) 1958 [St. Paul].

The authors used autogenous and homogenous veins, crimped braided nylon tubes, and compressed Ivalon sponge tubes for iliac-femoral arterial shunts or replacements in 24 patients and for femoral-popliteal arterial shunts or replacements in 73 patients. In the group of 24 patients, successful vein grafts existed more than 2 years in 7 of the 8 patients in whom they were used; the nylon tubes used at this level in 5 patients remained open for from 3 to 12 months. Of the compressed Ivalon prostheses used in the remaining 11 patients, 6 failed; the successful Ivalon sponge grafts were all patent over 14 months. In the group of 73 patients, vein grafts were used in 37, nylon tubes in 32, and Ivalon sponge prostheses in 4. Successful vein grafts existed 5 to 24 months after surgical treatment in 29 of the 37 patients. Sixteen of 32 nylon tube shunts were still open 3 to 12 months after the operation. The compressed Ivalon prostheses failed in all 4 patients in whom they were used. Thus, the most satisfactory results in patients with long segmental occlusions in the iliac-femoral and femoral-popliteal areas were obtained with the use of autogenous saphenous veins and braided nylon tubes, both as shunts and as replacements.

Of 20 patients with popliteal aneurysms, 11 underwent lumbar sympathectomy with subsequent resection of the aneurysm in 3, 1 had a simple resection of the aneurysm, and in 8 primary resection with autogenous vein grafting was attempted after sympathectomy. Sympathectomy followed by immediate resection appeared to be the most satisfactory method of treatment for the symptomatic or asymptomatic popliteal aneurysm. In 4 of the 8 patients in whom attempts at replacement with autogenous vein grafts were made, encouraging results were obtained in that these patients have functionally good extremities without claudication.

Short segment thromboendarterectomies were performed in 5 patients with acute arterial occlusions. Two of these were due to embolism and 2 to thrombosis. One of the 5 patients died within 24 hours after the operation, and autopsy revealed multiple emboli in the renal, splenic, and cerebral vessels. Another patient required a saphenous vein graft of the common femoral artery, since the remaining vessel after endarterectomy was too friable to hold sutures. This patient is well, with good peripheral pulses, 30 months after the operation. The remaining 3 patients had patent vessels on follow-up examination 3 months to 1 year after the operation. For short segments, and particularly in cases of acute occlusion, either by embolism or spontaneous thrombosis in severely sclerotic femoral arteries, endarterectomy is definitely necessary for a successful result.

Lung Resection in Tuberculosis. A. M. Dyhno. Vestnik. khir. 8:10-16 (March) 1958 (In Russian) [Leningrad].

The author reports on 127 patients with fibrocavernous tuberculosis who were operated on. There were 5 pneumonectomies, 72 lobectomies, and 50 segmental resections. The onset of the disease dated from 1½ to 14 years. All the patients were treated preoperatively with antibiotics, artificial pneumothorax, and sanatorium rest. There were 8.8% postoperative deaths, the cause being shock in 4 patients, hemorrhage in 2, and empyema in 2. The postoperative course was complicated in 4.9% by a bronchial fistula and in 12.7% by empyema.

Surgical Methods of Treatment of Tuberculosis of Children and Adolescents. M. L. Shulutko. Vestnik khir. 80:16-23 (March) 1958 (In Russian) [Leningrad].

Cavernous types of tuberculosis of children and adolescents give unfavorable prognosis when treated conservatively. The introduction of streptomycin and of other chemical therapeutic substances has not solved the problem. Surgical methods are beginning to play an important role in the complex treatment of children and adolescents with cavernous pulmonary tuberculosis. An analysis of 131 patients operated on gave a postoperative mortality of 3%; there was empyema in 2.3% and bronchial fistula in 3.8%. Follow-up revealed deaths from tuberculous process on the operative side in 2 patients. The remaining 120 patients (91.6%) are practically well and free from tubercle bacilli. Attention is called to the fact that the mediastinum in children and adolescents has considerable mobility. The author therefore advocates introduction of a pneumothorax 3 to 5 days before the operation. This results in gradual replacement of the mediastinum and in giving the general organism an opportunity to adapt itself to new conditions. Pulmonary resection is indicated for the following conditions: (1) in the presence of multiple cavities of the lung; (2) in patients with marked fibrosis surrounding a pulmonary cavity; (3) in the presence of tuberculous lesions and bronchiectasis; (4) in patients with bronchial stenosis; (5) in the presence of diffuse lobar infiltration after preliminary but ineffective antibacterial therapy; (6) in cases of caseation of the lung; (7) after prolonged but ineffective pneumothorax; and (8) after ineffective thoracoplasty, extrapleural pneumothorax, and oleothorax; employment in these patients of thoracoplastic procedures and of extrapleural pneumothorax is seldom successful. One of the peculiarities of the course of tuberculosis in children and adolescents is bilateral involvement. Of the 441 children treated in the author's clinic, 45 to 50% presented bilateral involvement. They were treated by artificial pneumothorax of one side and operative resection of the other side. The important problem in the treatment of bilateral tuberculosis is the maximal sparing of healthy tissue. This is best accomplished by a sparing bilateral resection.

Aneurysms of the Thoracic Aorta. F. H. Ellis Jr. Minnesota Med. 41:335-338 (May) 1958 [St. Paul].

The author reports on 24 patients, between the ages of 5 and 73 years, with aneurysms of the thoracic aorta which were arteriosclerotic in 10, syphilitic in 5, traumatic in 4, congenital in 2, mycotic in 2, and dissecting in 1. Resection of the lesion was done with the aid of hypothermia in 18 of the 24 patients. The main cause of inoperability was the location of the aneurysm in either the ascending aorta or its proximal arch. Grafts were used in 17 of the 18 patients on whom resection was done. Homografts were used in 14 patients, an Ivalon sponge graft in 2, and a crimped nylon tube in 1. Hypothermia was used as a means of avoiding ischemia of the spinal cord during cross clamping of the aorta. By reduction of the arterial oxygen requirement of the central nervous system, a safe period of aortic occlusion up to 1 hour is permitted. Six patients died in the first week after the operation. Hemorrhage, complications of hypothermia, or both accounted for most of the deaths. In only 1 patient were neurological signs and symptoms recognized in the postoperative period. Three other patients died later, and death resulted from hemorrhage in all. Aneurysm of the thoracic aorta is a serious threat to health and life, and its surgical removal should be considered seriously despite the high mortality rate.

Clinical Importance of Traumatic Fat Embolism. H. Kühne and K. H. Kremser. Beitr. klin. Chir. 195:385-394 (No. 4) 1957 (In German) [Munich, Germany].

Autopsies in 643 fatal traffic accidents during the years from 1954 to 1956 revealed fat embolism of the lungs in 95%; it was massive in 59%, and the systemic circulation was involved in 23%. Since autopsy findings indicate the terminal status and do not permit deductions regarding clinical conditions, the authors investigated the presence of air embolism in patients with comminuted and open fractures, in those with traumatic décollement, and in those subjected to fracture nailing. One hundred fifteen of a total of 2,956 patients with such injuries died, and whereas fat embolism was found in all of those who died, the clinical diagnosis of fat embolism was made during life in only 7 of the patients whose histories are presented. Five of these 7 patients had sustained severe traffic accidents, and the other 2 had fallen from great heights. They had sustained multiple fractures. In 1 case extensive décollement was associated with a pelvic fracture and fractures of the leg and femur.

All the patients were conscious on admission to hospital, but they were in shock. After measures were taken to counteract the shock, 6 patients responded with rapid recovery, but 5 died after intervals of from 1 to 4 days with signs of respiratory insufficiency. Case 7 is of particular interest, because pulmonary as well as cerebral symptoms indicated extensive fat embolization, but the patient apparently was able to cope with these emboli, because at the time of his discharge he was free from all neurological disturbances. The severe shock existing in all patients decided the therapeutic measures. Only 1 of the patients (case 7) could be given specific therapy in the form of dehydrocholic acid (Decholin) and eupaverin, whereas in the others death occurred so rapidly that there was no time for such treatment. In the further discussion of fat embolism, the authors consider not only the cases reported but also literature reports.

Cavernous Hemangiomas, "Cavernomas" of Liver. F. Niemann and W. Penitschka. Beitr. klin. Chir. 195:257-277 (No. 3) 1957 (In German) [Munich, Germany].

The authors report on a 44-year-old woman with cavernoma of the liver who was operated on at the surgical clinic of the University in Bonn, Germany. She had severe epigastric pain during the 7 months before surgical intervention and had lost a considerable amount of weight. Roentgenologic examination of the gastrointestinal tract, heart, lungs, and urogenital tract did not reveal any abnormality. Laparotomy revealed a partly nodulated and partly smooth tumor, the size of the head of a child, which partly adhered to the parietal peritoneum; it occupied the entire left epigastrium up to the umbilicus and was connected with the liver. There was a distinct border line between the diseased and the normal tissue of the liver. The left enlarged lobe of the liver which was entirely occupied by the tumor was resected. Microscopic examination of the surgical specimen revealed a typical cavernoma. The course of healing was delayed for 8 weeks by a seropurulent secretion which originated in a cavity below the left costal arch at the border of bone and cartilage, suggesting a cartilaginous necrosis. The patient was discharged in excellent general condition 10 weeks after the operation. She had gained 5 kg. (11 lb.).

One hundred two additional cases of surgically removed cavernoma of the liver were collected from the literature. Thirteen (12%) of these tumors had perforated. The primary mortality rate among patients operated on was 11%. The best operative results were obtained with the radical extirpation of the tumor, whether the tumor had ruptured or not. Despite the fact that hemostasis was frequently difficult, only 2.5% of the patients undergoing resection died, as compared with 90% of those in whom only tamponade was used for a perforating cavernoma. In 7 patients the size of the tumor decreased as a result of roentgenotherapy, injections promoting sclerosis, or galvanocautery. Late results of surgical treatment were reported in 16 of the 102 patients with cavernoma of the liver who were followed for 2 to 10 years; all of them were in good health and completely free of complaints. True recurrences were not reported.

A Further Description of the Pathologic Physiology of Congenital Megacolon and the Results of Surgical Treatment. R. B. Hiatt. Pediatrics 21:825-831 (May) 1958 [Springfield, Ill.].

The author reports follow-up results of 63 patients who were operated on for congenital megacolon at the Columbia-Presbyterian Medical Center, New York, between 1947 and 1955. There were 5 deaths, 3 of which occurred in infants whose age at the time of the operation was less than 12 months and were due to severe enterocolitis occurring from 3 months to 1 year after the operation. The 4th early postoperative death occurred also in an infant less than 12 months of age, and was due to acute aspiration in the nursery. The 5th death occurred in a child whose age at the time of operation was 18 months and who died at 3 years of age of acute membranous colitis. The 58 surviving patients had undergone a "pull-through" procedure, consisting of a surgical intussusception of the entire rectum and the lower two-thirds of the sigmoid through the anus, with replacement by more proximal colon and with an end-to-end anastomosis of the anus and sigmoid in one stage. Twenty-nine (50%) of these patients were completely continent immediately after the operation or within 1 year after the operation; 20 patients (34%) became completely continent within 2 to 5 years after the operation; and in 9 patients (16%) fecal staining or actual incontinence is still a persistent problem after many years. Careful observation of these 9 patients with imperfect anal control revealed that enterocolitis and psychological maladjustment are the 2 prominent factors which contribute to this difficulty.

In congenital megacolon one is dealing with a slowly progressive disease as a result of gradual development of hypertrophy in the proximal portion of the aganglionic segment of the colon; this hypertrophy in time increases the degree of obstruction, because its response to the constant physiological stimulus of feces occurs in the form of nonpropulsive spasm. This hypothesis explains why good initial results may be obtained from a segmental resection of the transitional segment, since, although only a part of the aganglionic segment is removed, the hypertrophied portion which is responsible for most of the obstructive element is removed. This initial good result, however, can only be temporary, since obstruction is bound to occur when hypertrophy develops again in the remaining achalasic segment. The replacement of the rectum and the lower sigmoid by proximal colon in patients with congenital megacolon has proved successful, as manifested by the long-term follow-up study.

NEUROLOGY & PSYCHIATRY

Barbiturate Narcomania as Problem in Medical Department with Resident Psychiatrist. E. Kåss, N. Retterstøl and T. B. Sirnes. Tidsskr. norske lægefor. 78:341-345 (April 15) 1958 (In Norwegian) [Oslo].

Of 3,750 patients admitted to a medical department with a resident psychiatrist during a 2-year period, 63 were drug addicts. Sixty patients (40 men, 20 women) were addicted to barbiturates alone or combined with other narcotics, 44 of them being admitted because of acute intoxication. In more than half of the cases there was also chronic alcoholism. Fifteen patients had had long-term treatment with narcotics prescribed for illness. In the remaining patients the main cause of the addiction was attributed to personality deficiency. More than half of the patients were without work. Abundant amounts of vitamins B and C were given, often combined with insulin in small doses. Some patients were also given ataraxics (chlorpromazine, reserpine, meprobamate). In general, treatment of narcomania cannot be carried out well in a medical department, where the treatment of somatic symptoms is important. The patients were prepared by the psychiatrist to be motivated, if possible, for a long-term treatment in psychiatric institutions. There are no possibilities for narcomaniacs unwilling to be treated. The prognosis for permanent recovery in established narcomania is unfavorable. Greater weight should be put on prophylaxis.

Primary Amyloidosis with Special Reference to Involvement of the Nervous System. R. A. Chambers, W. E. Medd and H. Spencer. Quart. J. Med. 27:207-226 (April) 1958 [Oxford, England].

Primary amyloidosis has been divided into cases in which there is 1 localized tumor and those in which the deposits are more generalized. The present paper describes 6 patients with the generalized forms, 3 of whom initially presented neurological problems. Various aspects of amyloidosis are discussed on the basis of these case histories and of literature reports. Approximately two-thirds of all cases occur in men, and the clinical form is partly related to age, neuropathy occurring relatively early and cardiac myopathy relatively late. The clinical picture varies but frequently shows the gradual onset without fever or toxemia, in adult life, of impaired function of the myocardium, kidneys, or peripheral nerves. The illness is progressive despite treatment and, if the heart or kidneys are involved, leads to death in a few years. The polyneuritis affects first and most severely the longest fibers. The symptoms are predominantly sensory, and usually the first symptom is pain, often lightning pains. The motor signs are those common to all types of chronic polyneuritis and may be of any severity. The characteristic sensory abnormality is diminished appreciation of temperature and pain. The ankle jerks, and later the other tendon reflexes, are lost, but they may be present when symptoms and cutaneous sensory signs are advanced. Additional clinical features include diarrhea, impotence, vitreous opacities, abnormal pupils, and thickened peripheral nerves.

That the diagnosis of amyloid neuropathy is difficult is demonstrated by the fact that chronic tonsillitis, dermatitis artefacta, hysteria, malingering, disseminated sclerosis, spinal tumor, tabes dorsalis, and leprosy were the diagnoses considered in the 3 patients who initially presented neurological problems. Amyloid polyneuritis may mimic tabes, but this diagnosis should be doubted if the motor symptoms are symmetrical and sphincter symptoms are absent. Examination of the blood and cerebrospinal fluid may be necessary. If leprosy is likely, the social consequences make biopsy essential. Sensory radicular neuropathy is similar in many respects, including the family history and, sometimes, diarrhea and abnormal pupils, but wasting and weakness and enlarged peripheral nerves, all characteristic of amyloid polyneuropathy, are usually absent. Serum protein examination, the Congo red test, and biopsy are valuable diagnostic aids. Serum protein changes include diminished total protein, diminished albumin, and increased globulin values and the finding on electrophoresis of an abnormal protein, which may appear in the urine, in the region of the $\alpha_2-\beta$ globulin bands. In five of the 6 reported patients the total protein content and the albumin content were reduced or at the lower limit of normal. The Congo red test was performed for 3 of the patients. The result was positive in case 3, equivocal in case 1, and negative in case 6; the authors accepted 90% retention of dye in 1 hour as positive. The result probably depends on the amount of amyloid and its affinity for Congo red, and, although a negative result is of no significance, falsely positive results are rare. The authors conclude that amyloidosis, whether primary or secondary, is a single disease process, with variations in distribution determined by such factors as inheritance, age, and sepsis.

Tuberous Sclerosis: Case Report. H. Mavor and G. A. Schumacher. J. Maine M. A. 49:179-182 (May) 1958 [Brunswick].

The patient, a 37-year-old woman, was admitted to the neurology service of the DeGoesbriand Memorial Hospital in Burlington, Vt., on July 16, 1957, in status epilepticus. The history obtained on admission was meager. The patient apparently had had intermittent convulsive seizures for many years and had been treated with Dilantin capsules. This medication had been omitted for 2 days prior to admission. The onset of repetitive seizures occurred approximately 1 to 2 hours prior to admission. When first seen the patient was having successive focal and generalized convulsive seizures, consisting of tonic and clonic movements of the right upper and lower extremities, with occasional spread to the left, associated with apnea and cyanosis and followed by hyperpnea, coma, and widely dilated, unreactive pupils. The seizures were controlled with a total of 910 mg. of phenobarbital sodium given intravenously in divided doses over a 2-hour period. The presence of facial skin lesions resembling adenoma sebaceum, convulsions, and the deteriorated state implying mental retardation suggested a diagnosis of tuberous sclerosis. Hints of a familial incidence were obtained in that the patient's son suffered from "spells" and had never been able to attend school.

Tuberous sclerosis or epiloia, one of several recognized neurocutaneous syndromes, has as its outstanding manifestation the triad of convulsive seizures, mental deficiency, and skin lesions. Over 450 cases have been reported. In hospitals and colonies for the epileptic, the incidence among new admissions appears to be approximately 1 in 200. The disorder is congenital, and strong heredofamilial tendencies are present. Two major hypotheses are (1) that it is a disorder of prenatal development, i. e., of embryogenesis (blastomatous in origin), and (2) that it is actually a slowly progressive neoplastic process. One view has held that tuberous sclerosis and neurofibromatosis are similar, the former a central, the latter a peripheral neurospongioblastosis. Attention is usually called to the disease by the occurrence of convulsive seizures of both the major generalized type and the minor petit mal variety early in life. The coexistence with convulsions of mental deficiency and the characteristic butterfly distribution of small skin nodules, spreading from the nose over the cheeks and usually also involving chin and forehead, is sufficient to make the diagnosis. The brain in epiloia reveals grossly firm white nodules at the surface as well as deep in the cortex. Similar foci appear in the subcortical white matter. Tumor nodules may project into the ventricular cavities. Less often, nodules are also found in the basal ganglions, brain stem, and cerebellum. No specific therapy for the basic disease process is available. The usual anticonvulsants are employed to counteract seizure activity.

Is Cortisone Contraindicated in the Acute Phase of Polioencephalitis? R. De Mattia and F. Di Nola. Minerva med. 49:1183-1187 (March 31) 1958 (In Italian) [Turin, Italy].

The authors believe that cortisone may be used effectively in the management of acute polioencephalitis when the functional blockage can be ascribed to the compressive action of edema and is thus at least partially reversible. Cortisone was given to 8 patients with polioencephalitis in 6 of whom the disease was accompanied by tetraplegia and by paralysis of the bladder muscles. Paralysis of respiratory and of swallowing muscles affected 2 patients, and paralysis of respiratory muscles alone affected 2. Cortisone was given parenterally to all patients, 3 of whom received it in a single dose in combination with hydrocortisone (25 mg.) by the intrathecal route. Total dosage of 450 to 900 mg. of cortisone was administered in decreasing divided daily dosages, from 200 mg. in the beginning to 100 mg. at the termination of treatment, for a period of 4 to 6 days. Six of 8 patients survived with fair chances of functional restoration. The results were good, although they may be only partially attributed to the effect of cortisone.

GYNECOLOGY & OBSTETRICS

Intra-Aortic Transfusion: Discussion of Technic and Report of Five Cases. H. L. Riva, J. L. Breen, R. P. Hatch and W. L. Pickhardt. Obst. & Gynec. 11:537-542 (May) 1958 [New York].

Five women, between the ages of 28 and 43 years, 2 with spontaneous rupture of the uterus associated with intrauterine pregnancy, 2 with ruptured ectopic pregnancy, and 1 with carcinoma of the uterine cervix, who underwent abdominal surgery, were in severe shock and responded inadequately to intravenous transfusion of blood. The abdominal aorta then was used as a site for transfusion. By displacing the intestinal tract onto the abdominal wall, rather than packing it, time was saved and better exposure of the aorta was obtained. The transfusion was carried out with an angulated aortic needle, which was inserted just above the bifurcation of the aorta. Exposure of the aorta was performed by vertically splitting the posterior peritoneum to allow better exposure for placing the needle and for repair of the vessel, if the need should arise, thus avoiding concealed retroperitoneal hemorrhage. Hemorrhage was controlled by clamping either the aorta or the common iliac arteries with vascular clamps.

Intra-aortic transfusion of about 500 cc. of blood brought about a rapid change in all the patients, with complete stabilization of blood pressure occurring within 5 to 20 minutes. In addition, the immediate perfusion of the coronary and cerebral vessels was of great importance at the time of intra-aortic transfusion. Intra-aortic transfusion was accomplished in each patient within several minutes. The danger of air emboli was avoided by discontinuing the transfusion just before its completion. In none of the patients was it necessary to repair the aorta after the transfusion, and no retroperitoneal hematomas were observed. There was no morbidity or mortality in this small group of patients. The aorta at the time of abdominal surgery is easily accessible for transfusion and has many advantages over other arterial vessels. Intra-aortic transfusion is simple and requires a minimum of equipment. It is of unquestionable value in many cases in which death from hemorrhage seemes inevitable.

Mumps Mastitis in the Nursing Female, with a Case Report. R. J. Weaver and T. Neal Petry. J. Indiana M. A. 51:644-648 (May) 1958 [Indianapolis].

A 28-year-old woman was first seen on March 11, 1956, complaining of swelling and tenderness of her right jaw for 1 day. She was the mother of 3 children, 2 of whom had had mumps 2 weeks before, and the third and youngest was a nursing infant of 11 weeks. She returned 8 days later because her baby had "choked" while nursing. She said that 3 days after the previous visit her breasts had become very tender and swollen, but not hot. In a few days lactation decreased, and the physician thought this accounted for the infant's choking. At the second visit her left parotid was swollen, and she was ordered to cease nursing the child. The administration of stilbestrol, 0.1 mg. daily, was started, and 3 days later lactation had ceased, with caking of the breasts absent 6 days later. The infant was followed closely but manifested no signs or symptoms of mumps.

Although mumps mastitis is a recognized complication of epidemic parotitis, it has been reported rarely. The authors found reports of only 2 other cases, and only 1 of them concerned a nursing mother. Neither the infant of this patient nor the infant of the nursing mother cited had signs of mumps. The immunity existing in infants up to 6 or 8 months of age is generally considered passive immunity from the transfer of maternal antibodies across the placenta. The mothers were not immune in these 2 instances, and presumably the maternal circulation carried no antibodies. Therefore, the mechanism of the immunity displayed by the infants is apparently different. An alternate possibility is that the infants had subclinical mumps. The authors suggest that serologic tests be done on apparently well infants whose mothers have the disease, and that observations be made and reported as to whether nursing mothers with mumps mastitis can nurse after subsequent pregnancies.

Testosterone Pellet Implants for Advanced Breast Carcinomatosis in the Female: Preliminary Report. C. P. Lamar and P. R. Rezek. J. Am. Geriatrics Soc. 6:397-404 (May) 1958 [Baltimore].

The authors report on clinical and pathological observations made during a 10-year period at the Jackson Memorial Hospital, Miami, Fla., on 100 women who were treated by subcutaneous implants of testosterone pellets for palliation of advanced and otherwise intractable breast carcinomatosis. Testosterone (pure crystalline) compressed pellets (75 mg. each) were implanted, 10 at a time, into the subcutaneous fat through a special trocar. Implants were made at weekly intervals for 6 or more times. Then they were spaced farther apart—up to twice a year in a patient who survived for more than 8 years, and 3 to 6 times a year in other patients who survived for periods ranging from 3 to 6 years. Implants of pure testosterone have the advantage of more prolonged effect and less frequent administration than intramuscular injections of testosterone esters. Masculinizing changes seemed to be less conspicuous than with other forms of less intense androgenic therapy. Edema was minimal, and there was no hypercalcemia. In 2 patients tetanic muscular contractions were relieved by parenteral administration of calcium. As a rule, serum levels of protein, calcium, phosphorus, and alkaline and acid phosphatase remained within normal limits. Exacerbations of neoplastic activity were accompanied occasionally by a transient increase in the serum levels of alkaline and acid phosphatase, and more frequently by an increase in serum protein-bound iodine concentration and radioactive iodine uptake by the thyroid gland along with decreased glucose tolerance. Subjective responses were good in more than 90% of the patients, as manifested by reduction or even suppression of severe pain, production of euphoria, and gain in appetite, weight, and strength. The duration of remissions was variable, averaging 28 months, with a range of 8 weeks to more than 8 years.

The cases of 3 of the 100 patients are described to illustrate some gross and histological changes observed and the relatively low incidence of masculinizing changes. In a patient whose remission has persisted for more than 8 years, mammary biopsy was performed both before and after a radical mastectomy 3 years after onset of therapy. There was gross reduction in the size of the primary breast tumor and lymph nodes, but the histological picture showed no changes. In another patient impressive histological changes took place after androgenic therapy; there was remarkable new epithelization of all ulcerated areas with distinct healing and shrinkage of all lesions. Sex chromatin was observed in some of the tumor cells both before and after treatment; and again at autopsy, after hypophysectomy, sex chromatin was found in the skin, adrenal cortex, and tumor tissue.

Tuberculosis of the Endometrium: A Report on 250 Cases with the Results of Drug Treatment. A. M. Sutherland. Obst. & Gynec. 11:527-536 (May) 1958 [New York].

Two hundred fifty women, between the ages of 16 and 53 years, with endometrial tuberculosis, were treated at the David Elder Infirmary in Glasgow during the past 7 years. Twenty-eight patients were unmarried, and only 29 gave a history of previous pregnancy. A history of definite or possible extragenital tuberculosis was obtained from 137 of the 250 patients. The interval between the earlier tuberculous manifestations and the discovery of the endometrial infection varied widely but was 5 or more years in most of the patients. Principal symptoms consisted of infertility in 104 patients, abdominal pain in 54, profuse and sometimes irregular bleeding in 41, amenorrhea in 25, and vaginal discharge in 12. Fourteen patients had no complaints. Chest roentgenograms revealed unsuspected active pulmonary lesions in 8 and healed pulmonary lesions in 103. Cervical biopsy revealed unsuspected cervical tuberculosis in 4 patients. A provisional diagnosis of endometrial tuberculosis was based initially on the histological findings in the curettings in most patients. Bacteriological proof was sought in 229, and a positive result was obtained in 170. In 132 of the latter patients, the tubercle bacilli were of the human type. Antituberculous agents were given to 242 patients. Streptomycin and aminosalicylic acid (PAS) were given for 84 days to 152 patients. Of these, 102 (67%) had a persistently negative endometrium after an average follow-up period of 25 months, 32 (21%) had recurrences of the endometrial infection, and 18 were lost to follow-up. Streptomycin and isoniazid were given for 84 days to 69 patients. Fifty-nine patients remained negative after an average follow-up period of 16 months. Recurrences were observed in 6 patients in the second and the third year after treatment. Four patients were lost to follow-up. Aminosalicylic acid and isoniazid were given to 19 patients for 6 to 12 months. It is still too early to compare the results obtained with those in the other groups. Two patients were treated with isoniazid alone, but the use of a single drug is undesirable and this method was abandoned. Recurrences occurred in 40 of the 242 patients, and 22 of the 40 patients were cured after a second course of drug therapy, the average time of follow-up being 22 months. Toxic drug reactions, such as vestibular disturbances, skin rashes, and gastrointestinal disturbances, occurred in 35 (14%) of the 242 patients, requiring discontinuation of therapy in all these patients.

From a consideration of the results of treatment obtained in these patients, it appears that the results obtained are better than those observed in control patients. It is too early to assess the value of streptomycin and aminosalicylic acid as compared with that of streptomycin and isoniazid, although the results to date suggest that the latter combination is at least as effective as the other and is less likely to be associated with toxic drug reactions. The occurrence of major drug reactions in 35 patients is disturbing. Although a few control patients did become negative without chemotherapy, the reported data show that it is not justifiable to withhold treatment from any patient with proved endometrial tuberculosis. Most of the controls remained positive at follow-up, and an appreciable number showed clinical deterioration in the course of the control year and required immediate treatment. In contrast to that, most of the treated patients have been cured of their principal complaints, apart from those with infertility. A continued follow-up of the patients will show whether these conclusions should be modified in the light of further experience.

Postclimacteric and Menopausal Hemorrhages. G. F. Winter, R. Häntsch and P. Rotter-Pool. Ztschr. Geburtsh. u. Gynäk. 150:19-28. (No. 1) 1958 (In German) [Stuttgart, Germany].

The authors regard as the postclimacteric phase the period between the last menstruation and the definite menopause, defining the onset of the latter as 3 years after the last menstruation. They admit that the definition of these 2 concepts varies in the literature, and since they wanted to compare their findings with those of other clinics, they limit the postclimacteric period in this study to 2 years after the last menstruation. They investigated the postclimacteric and menopausal hemorrhages of patients treated at the University Women's Clinic in Berlin during the 5 years from 1950 to 1954 inclusive. A total of 1,623 patients were involved. It was found that 57.5% of the postclimacteric and menopausal hemorrhages were due to malignant lesions, whereas the average in the world literature is 53.7 or 55.2%. Malignant lesions were the cause of 35% of the genital hemorrhages during the postclimacteric and of 60% of those during the menopausal period, whereas in sexually mature women, up to the age of 45, a total of 15% of the nonmenstrual hemorrhages were due to malignancies. Cervical carcinoma was found to cause 66%, carcinoma of the body of the uterus 22%, and carcinoma of the ovary 5.7% of all the postclimacteric and menopausal hemorrhages that were due to malignant causes.

Studies on the incidence of hemorrhage in the presence of ovarian tumors revealed that 34% were accompanied by hemorrhage, or abut 1 in 3. An ovarian tumor was found, on the average, in 1 woman in 17 with postclimacteric or postmenopausal hemorrhages. Cervical polyps were the most numerous among the nonmalignant lesions responsible for genital hemorrhages, accounting for 16.2% of the postclimacteric or menopausal hemorrhages traceable to benign causes. One of 3 "benign" postclimacteric hemorrhages originated in the endometrium under hormonal stimulus, whereas only 1 in 9 of the menopausal hemorrhages was due to this cause. In 40% of all the women with bleeding from a hormonally activated endometrium, the history revealed treatment with estrogens. The percentage was even higher (50%) when the women were questioned regarding the use of hormone ointments and creams. Myoma, which together with glandular hypertrophy is the most frequent cause of hemorrhages during the climacteric, plays only a subordinate role in this respect during the postclimacteric period and during the menopause, accounting for 6.2% of benign and for 2.6% of all hemorrhages.

PEDIATRICS

Serum Oxaloacetic Transaminase Activity in Acute Rheumatic Fever: Values in Cases With and Without Salicylate Therapy. R. W. Massie and M. Stahlman. A. M. A. J. Dis. Child. 95:469-476 (May) 1958 [Chicago].

Eighteen patients with acute rheumatic fever were studied over long periods with serial determinations of serum glutamic oxaloacetic transaminase (SGOT) activity, C-reactive protein (CRP), antistreptolysin-O (ASO) titer, and erythrocyte sedimentation rate (ESR). SGOT activity was elevated in some patients with acute rheumatic fever. These elevations were inconstant, however, and equally ill patients sometimes showed no elevation. Elevated values of SGOT occurred only in the patients with active rheumatic carditis. Rheumatic carditis was frequently not accompanied by elevation in SGOT. A single determination of SGOT activity was of little value in diagnosing acute rheumatic fever or in following the course of the disease. Some values that were not above the "upper limit of normal" were demonstrated to be significantly elevated when serial determinations were performed. A rise and fall in SGOT values were often well correlated with ESR, CRP, and ASO-titer determinations as well as with the clinical status of the patient. Administration of acetylsalicylic acid did not affect SGOT activity in the absence of active rheumatic carditis. The effect of salicylates on SGOT activity in the presence of active rheumatic carditis was uncertain, and inconstant results were obtained in several patients.

Bilateral Choanal Atresia, a Surgical Emergency in the Newborn. R. C. Morrow. J. Maine M. A. 49:135-136 (April) 1958 [Brunswick].

Some cases of neonatal asphyxia are due to undetected bilateral congenital atresia of the posterior nares. The author presents observations on 4 infants with bilateral atresia observed at the Mary Fletcher Hospital in Burlington, Vt., and reviews the recent literature on this problem. The fact that the 4 cases were observed in 3 years suggests that this defect cannot be regarded as rare. The persistence of the nasobuccal membrane, which normally ruptures in the 7th week of fetal life, is the most widely accepted embryologic mechanism of this anomaly. The newborn infant is often unable to survive nasal obstruction, as though it were not instinctively aware of the simple expedient of breathing through the mouth. The clinical picture is that of obstructed breathing, with the varying degrees of intermittent success in getting a little air through the mouth. Usually the infant can be kept breathing by any expedient which serves to hold the mouth open and the tongue down and forward. Feeding is difficult, because sucking, swallowing, and breathing cannot be carried on simultaneously. Even infants who can achieve mouth breathing are in danger of death by starvation. Once the condition is suspected, the diagnosis can be clarified by attempting to pass catheters through the nasal cavities into the pharynx, and by obtaining x-ray films with the instillation of contrast media into the nostrils.

Every breath of the infant should be supervised until adequate surgical relief is achieved. The mouth can be kept open by means of a small oral airway of the type used in anesthesia. The surgical management is early penetration of the choanal obstruction. Three of the 4 newborn infants with bilateral choanal atresia observed by the author were operated on, on the 1st, 2nd and 16th day of life respectively. The 4th infant had, in addition, multiple anomalies of the heart and great vessels and died on its 9th day. The choanal problem was recognized, and, by constant nursing attention, oral breathing and adequate feeding were being maintained, while corrective surgery was to have been done had the infant survived its cardiac anomalies a few more days. The 3 infants responded well to prompt operation in the newborn stage, followed by a program of periodic dilatations and the intermittent use of polyethylene breathing tubes. The possibility of bilateral choanal atresia should be thought of in threatened neonatal asphyxia.

Acute Cerebellar Ataxia of Childhood: Report of 9 Cases. G. King, G. A. Schwarz and H. W. Slade. Pediatrics 21:731-745 (May) 1958 [Springfield, Ill.].

The authors report on 6 boys, between the ages of 2½ and 11 years, and on 3 girls, between the ages of 17 months and 3 years, with acute cerebellar ataxia. The neurological sign of most clinical significance was the ataxic gait. This occurred in varying degrees of severity in 8 of the children. Truncal ataxia, action tremor, and dysmetria were also frequently noted, but nystagmus, hypotonia, and hyporeflexia were infrequently observed. Choreiform movements and hemiparesis with hyperreflexia occurred in a few patients and indicated that the pathological process was not limited to the cerebellum in these patients. Fever was present in 5 patients. Seven of the patients had some degree of disturbance of personality and state of consciousness as part of the illness. The most pressing diagnostic problems presented were the degree of increased intracranial pressure and the possibility of a neoplasm of the posterior fossa. Changes of the optic nerve heads in 4 patients and bilateral early evidence of papilledema in 2 were suggestive of increased intracranial pressure. The indications were such that ventricular tap and ventriculography were performed in 5 of the 9 patients; in none of them was the intraventricular pressure increased. Five patients made a complete recovery. Residual disturbances in behavior were observed in 4 children: there was simple retardation in 1 and a schizoid personality change requiring institutionalization in another; in the remaining 2, only mild apathy and irritability at school were reported. The causation was not determined in any of the 9 patients. The children were quite healthy when the acute ataxia began, and none of them had a history of head trauma or preceding infection. Four of the patients had the onset of their illness in the months from January through March, and 5 in the months from August to October; these findings might suggest that these cerebellar disorders of childhood are due to different seasonally prominent pathogens.

Similar cases were collected from the literature, which had been recorded as "acute cerebellar encephalitis" or "acute cerebellar ataxia," a form of nonsuppurative encephalitis. The concept is proposed that these cases represent a toxi-infectious process of variable causation with the cerebellum or its systems as the major or only target organ. The main significance of these relatively benign forms of cerebellar disorder in children is their differentiation from cerebellar tumor. In the cerebellar medulloblastoma, the course is inevitably progressive with increasing papilledema or hydrocephalus. In acute idiopathic cerebellar disorders, the papilledema does not increase; there is usually no progression of signs, and in several weeks the signs begin to recede. A careful, watchful waiting would seem to be the best procedure in such cases, but ventricular tap and ventriculography may be the methods of choice in settling the diagnostic problem finally.

Multiple Sclerosis in Children: A Clinical Study of 40 Cases with Onset in Childhood. J. C. Gall, A. B. Hayles, R. G. Siekert and H. M. Keith. Pediatrics 21:703-709 (May) 1958 [Springfield, Ill.].

The authors studied 26 girls and 14 boys with disease of the central nervous system, characterized by several attacks of neurological dysfunction and disseminated lesions, with onset in childhood and clinically typical of multiple sclerosis. In 8 of the 40 patients who were admitted to the Mayo Clinic between 1920 and 1952, the age at the onset of the disease was 10 years or less, and in the remaining 32 it was between 11 and 14 years. The disease as it occurred in these children did not appear to differ clinically from the disease as observed in adults, in respect to mode of onset, symptoms, physical findings, and changes in the cerebrospinal fluid. In contrast, however, to the equal occurrence of multiple sclerosis in men and women according to reports on adults by other workers, the girls predominated among these children in a ratio of 2:1. Follow-up data were available by letter on 32 patients; 10 were still ambulatory, 10 were bedfast, and 12 had died. Death presumably resulted from multiple sclerosis or its complications. The youngest patient to die was 16 years old. A pediatrician confronted with a child showing evidence of scattered neurological deficits that remit, particularly a disturbance of vision and coordination, should consider the possibility of multiple sclerosis.

Acute Epiglottitis in Childhood: A Serious Emergency, Readily Recognized at the Bedside. W. Berenberg and S. Kevy. New England J. Med. 258:870-874 (May 1) 1958 [*Boston*].

The authors report on 26 boys and 16 girls, between the ages of 3 months and 14 years, with epiglottitis, who were admitted to the Children's Medical Center in Boston between 1946 and 1954. The onset of the disease was abrupt, and in 39 patients the initial complaint was one of difficulty in breathing. In patients who were able to express themselves, extreme pain in the throat was impressive and usually associated with marked dysphagia. There was a striking retention of secretions, with visible and copious puddling of pharyngeal mucus in 20 patients. Irritability and marked restlessness appeared fairly early. Hoarseness was present in 12 patients at the time of admission to the hospital. Definite stridor occurred in 30 children. A croupy crow was described in 15. Temperatures ranged between 100 F (37.7 C) and 105 F (40.5 C), with an average of 102.5 F (39 C). The respiratory rates varied between 22 and 60 respirations per minute. There was definite involvement of the epiglottis in all the patients. Although this varied somewhat in severity and in the apparent degree of inflammation, constant features were edema and a striking, fiery-red appearance, so that on depression of the tongue and examination of the pharynx, a "cherry-red" epiglottis came into view of the examiner. Diminished breath sounds indicated poor air exchange in 24 patients. A history of prostration and marked respiratory obstruction was obtained in the 3 patients who were found to be dead on arrival at the hospital. Two additional children died within 3½ hours after admission.

Blood cultures were obtained in 16 of the 39 patients who were alive at the time of admission to the hospital. Positive cultures for Hemophilus influenzae, group B, were obtained in 11 of the 16 patients. One blood culture yielded pneumococci. Throat culture yielded H. influenzae, group B, in 17 patients and a hemolytic Staphylococcus pyogenes var. aureus in 2. Direct cultures from the epiglottis at the time of tracheotomy, which was carried out on 18 patients as a lifesaving measure, yielded pneumococci in 1 patient, beta-hemolytic streptococci in 1, and H. influenzae, group B, in 11. Penicillin and streptomycin were given to 16 patients, penicillin, sulfadiazine, and streptomycin to 10, streptomycin and sulfadiazine to 5, penicillin, streptomycin, and chloramphenicol to 2, penicillin and sulfadiazine to 1, penicillin and chloramphenicol to 1, all four agents to 1, and chlortetracycline and chloramphenicol to 1. Penicillin and streptomycin were administered intramuscularly for 24 hours, and then orally as soon thereafter as the patient could tolerate that route. Sulfadiazine was given orally, subcutaneously, and, to 3 patients, intravenously.

Acute epiglottitis is a serious and often fatal condition that, although infrequently recognized, lends itself to accurate bedside diagnosis with consequent institution of specific lifesaving therapy. Its recognition and management should become familiar to all concerned with the care of sick children. The reported data emphasize the importance of H. influenzae, group B, as the predominant but not the only micro-organism producing this clinical picture, and the lifesaving value of tracheotomy to relieve the rapidly developing obstruction of the upper airway. The chemotherapeutic agent of choice is chloramphenicol in doses of 100 mg. per kilogram of body weight given intravenously for the first 24 to 36 hours and then reduced to 50 mg. per kilogram orally if it is tolerated.

Diabetes and Growth in Children: Comments on the Mauriac Syndrome and Its Treatment. H. Lestradet. Presse méd. 66:582-584 (April 2) 1958 (In French) [Paris].

The appearance of a significant insulin deficiency in children during the period of growth may give rise to clinical manifestations which should be given individual consideration. One of these clinical forms, presented only by patients capable of significant adrenocortical response, is the Mauriac syndrome, in which retardation of growth may or may not be associated with evident signs of hypercorticism. Retarded growth and delay in puberty in juvenile diabetic patients, however, should be ascribed solely to nutritional deficiency and to a poorly regulated insulin therapy, and not to a metabolic derangement peculiar to the disease itself. In some of the author's patients with the Mauriac syndrome, a slight increase in the dietary supply of glucides was followed by a dramatic regression of hepatomegaly, resumption of growth, and a rapid onset of puberty.

Treatment then consists of (1) a normal, well-balanced diet, with a sufficient supply not only of proteins and vitamins but also of glucides, and (2) a well-supervised insulin therapy. Twice the average dose of insulin required by diabetic adults may be needed by children with diabetes, if they are to have a satisfactory physiological development during the period of puberty. Thereafter these large doses of insulin can be reduced, sometimes rapidly, to those usually regarded as normal in adults. Regular insulin is sometimes poorly tolerated by children with the Mauriac syndrome. Thus, no improvement was obtained from total doses of 120 to 140 units of regular insulin administered in 6 injections daily to a 10-year-old boy in whom ketosis and hypoglycemic reactions occurred alternately. The administration of 2 injections daily of 30 to 40 units (one-third of the previous dose) of protamine zinc insulin, however, resulted in the immediate disappearance of ketosis and hypoglycemia, while at the same time the hepatomegaly disappeared and growth was resumed. Six months later this patient had grown 6 cm. (about 2½ in.) in height, and the usual treatment with a mixture of regular insulin and protamine zinc insulin administered in a single injection in the morning could be resumed. Delay in growth, whatever clinical aspect it assumes as a result of individual hormonal reactivity and of the degree of insulin insufficiency, should disappear completely if children with diabetes are treated according to physiological therapeutic principles, i. e., if they are given a rational diet and insulin therapy adapted to their needs, which are generally great during the period of growth.

Intestinal Diseases After Antibiotic Therapy: Clinical and Bacteriological Aspects of Bacterial Superinfection After Treatment with Broad-Spectrum Antibiotics. G. Möbius, L. Möbius and L. Weingärtner. Ztschr. Kinderh. 80:615-641 (No. 6) 1958 (In German) [Berlin].

The authors list 5 groups of secondary effects that may occur after treatment with broad-spectrum antibiotics, particularly after penicillin, streptomycin, chloramphenicol, chlortetracycline (Aureomycin), and oxytetracycline (Terramycin). These are (1) toxic effects, (2) allergic complications, (3) damage to the hematopoietic system, (4) bacteriolysis-induced secondary effects resembling the Herxheimer reaction during syphilis therapy, and (5) complication resulting from effects on the physiological bacterial flora in the respiratory or intestinal tracts. This paper is especially concerned with observations on 13 children, in whom serious intestinal disturbances developed during treatment with broad-spectrum antibiotics. High temperatures, watery stools, and vomiting occurred from 4 to 11 days after onset of the antibiotic therapy. All except 1 of the children were less than 2 years, and 7 were less than 1 year old. Eight of the children died, and 5 survived. All except 1 child had been treated with chloramphenicol, a few had received penicillin or chlortetracycline in addition, and 1 had received only chlortetracycline. The feces or intestines of all the children contained resistant staphylococci, and in 2 of the infants who died pathogenic fungi (Candida and Aspergillus) were found in addition.

On the basis of clinical, bacteriological, and pathological investigations on the 13 patients and of a review of literature reports, the authors emphasize that intestinal disorders after treatment with broad-spectrum antibiotics are to be characterized as superinfections, which are produced most frequently by staphylococci that are resistant to antibiotics and occasionally by saprophytes that may become pathogenetic or by fungi. The causal organism that is resistant or not responsive to antibiotics originates in the physiological, oral, or intestinal floras, in which it becomes dominant and unrestrained after the selective elimination of susceptible organisms. The resistant staphylococci are often transmitted to the patient within the hospital, because here they are usually predominant. While the pathological changes in the intestine vary, they are usually characterized by a pseudomembranous inflammation. As an unexpected and hitherto not described finding, the authors observed in 3 of the children severe edema in the cecum, which on histological examination was found to be restricted to the submucosa, where it had caused extensive dissolution of fibers. This tissue-destructive edema is regarded as a manifestation of a disturbance in permeability with formation of an exudate high in protein content and with fermentative effect. The effect of the intestinal disorder on the body in general usually becomes evident in symptoms of the central nervous system. Edema of the brain, central follicular necrosis of the spleen, and fatty degeneration of the liver are generally found and are attributed to the action of staphylococcic toxins. However, septicopyemia could be excluded in the reported cases.

Retrolental Fibroplasia: A Case Report on Preventable Blindness. W. H. Havener. Ohio M. J. 54:496 (April) 1958 [Columbus].

The boy whose history is presented weighed 3 lb. 15 oz. (1,800 Gm.) at birth, the estimated length of pregnancy being 7 months. Oxygen was given for 3 days in unknown concentration. Although both eyes were normal shortly after birth, at the age of 6 months this child had markedly impaired vision. Reexamination at this time showed traction bands which displaced the large central retinal vessels. Fibrovascular membranes swept across the macular area, obviously destroying central vision. Retrolental fibroplasia occurs almost exclusively in premature infants who have received supplemental oxygen. Central vision may be destroyed by fibrovascular membranes, as in this case, or the whole retina may become detached and pulled forward to produce the "retrolental" membrane. No therapy is known to be effective once the disease has manifested itself. It is extremely hazardous to use oxygen in the care of premature infants, except when obvious cyanosis or other evidence of anoxia exists.

THERAPEUTICS

Acute Glutethimide (Doriden) Poisoning: The Use of Bemegride (Megimide) and Hemodialysis. G. E. Schreiner, L. B. Berman, R. Kovach and H. A. Bloomer. A. M. A. Arch. Int. Med. **101**:899-911 (May) 1958 [Chicago].

Glutethimide has been used widely as an hypnotic and a sedative. Chemically, glutethimide is α-ethyl-α-phenylglutarimide. While working with a new barbiturate antidote, β-methyl-β-ethylglutarimide, known as bemegride (Megimide), the authors were impressed by the clinical similarity and disparate pharmacology of α-ethyl-α-phenylglutarimide, the depressant, and β-methyl-β-ethylglutarimide, the stimulant. Shortly thereafter they had the opportunity of contrasting the response to glutethimide in barbiturate poisoning to the clinical response in a patient who was admitted with presumed barbiturate intoxication but proved subsequently to have negligible amounts of barbiturate and a substantial concentration of glutethimide in the serum. The authors describe their observations on 6 patients with severe glutethimide poisoning whom they treated with varying combinations of supportive measures, bemegride, and external hemodialysis. There was 1 fatality. The first patient, who had severe poisoning from the ingestion of 7.5 Gm. of glutethimide responded dramatically to bemegride. The second patient, who presumably had taken approximately 10 Gm. of glutethimide and possibly a small amount of secobarbital (Seconal), also responded immediately to bemegride. The depression of respiratory rate in this patient was extreme. It may have been related to the associated barbiturate intake or to the ingestion of alcohol or some other unknown drug.

The 3rd patient was admitted unresponsive after the ingestion of 10 Gm. of glutethimide. She also had taken alcohol and possibly other drugs. This patient died. A surprise finding at autopsy was the presence of a massive coronary atherosclerosis, which must be considered most unusual in a 24-year-old woman. The authors wonder whether circulatory impairment could have contributed to her death. The 4th patient had marked hypotension, even after return of a reasonable degree of consciousness in response to bemegride. There was also the possibility of chronic cumulative toxicity of glutethimide, since she appeared groggy before her acute ingestion. She demonstrated apnea on manipulation. Anoxemia worsened the coma, and this patient might not have survived without hemodialysis, which reduced the blood glutethimide level. Patients 5 and 6 were treated with bemegride, and in the latter hemodialysis was also used. The authors stress the difficulties of treating patients poisoned by drugs. The great variety of tranquilizing drugs and the numerous hypnotics and sedatives produce a great multiplicity of possible interrelationships of drug effects. The toxicologist dealing with patients must take cognizance of such factors as inaccurate history of dosage, ratio of ingested dose to absorbed dose, time elapsed before treatment, underlying physical state, and individual drug tolerance.

The authors define the bemegride-glutethimide relationship as a functional antagonism. Bemegride stimulates the respiratory and circulatory center and restores reflexes and consciousness. However, the drug also produces exaggerated reflexes, muscle twitching, tremor, clonus, hyperventilation, and epileptic potentials in the electroencephalogram. Discussing a therapeutic plan for acute glutethimide intoxication, the authors show that, in patients with the mild form, symptomatic therapy and patience are enough. In patients with a moderate degree of intoxication, treatment should include lavage of the stomach. The use of endotracheal suction and oxygen and pressor drugs for hypotension are valuable, but care is necessary to avoid overhydration. Cerebral edema represents a major threat. It is well to be suspicious if more than 1,500 mg. of bemegride is required to lighten anesthesia. The administration of bemegride should be stopped immediately if clonus or convulsions are produced. Patients with severe glutethimide intoxication should be titrated with bemegride immediately after a sample has been taken for the determination of glutethimide blood level before bemegride is given. In the event of failure to elicit a light reflex or plantar withdrawal, a bemegride requirement greater than 1,500 mg. on titration, convulsions from bemegride, or later deterioration of the clinical state, plans should be made for external hemodialysis.

On the Mechanism of the Diuretic Action of Chlorothiazide in Human Beings. V. Bonomini and P. Zucchelli. Policlinico (sez. prat.) **65**:487-496 (March 31) 1958 (In Italian) [Rome].

Diuretic action of chlorothiazide was studied in 19 patients of both sexes, between the ages of 19 and 68 years. Cardiovascular or renal disorder was present in 9 patients, cardiac decompensation of the congestive type in 6, and edema in the lower extremities ascribed to chronic kidney disease but unrelated to hyperazotemia in 4. Chlorothiazide was administered intravenously in a single injection, varying from 100 to 500 mg., without causing toxicity. Chlorothiazide produced an increased urinary output in patients with cardiovascular disorders, but only a slight effect in patients with a renal disorder. Larger doses of the drug had an effect on duration of the action rather than on its intensity. Chlorothiazide did not affect either the glomerular filtration rate or the renal blood flow. The drug exerted its diuretic effect only through the tubular action. Like mercurial diuretics, chlorothiazide blocked the reabsorption of sodium chloride. The drug also produced an increased excretion rate of phosphate, bicarbonate, and sodium chloride. It caused a decrease in both ammonia and titratable acidity excretions. The pH of the urine increased in patients with cardiovascular decompensation, but it did not change much in patients with severely damaged renal tubules. Diuretic response to chlorothiazide resulted from blockage of sodium chloride reabsorption in the renal tubules. This study confirms the effective diuretic action of chlorothiazide in human beings.

Sodium Balance During Prednisone Treatment. S. Gjørup and J. H. Thaysen. Ugesk. læger 120:471-476 (April 10) 1958 (In Danish) [Copenhagen].

Prednisone is not suitable as the only substitution therapy in Addison's disease. It is particularly adapted for long-term treatment in cases where cortisone has caused troublesome fluid retention or where cortisone has been regarded as contraindicated because of edema or tendency to edema. No potassium addition should be given during treatment with prednisone. Although with the usual doses applied in the treatment of chronic polyarthritis and with free choice in diet the development of a salt-poor syndrome is hardly to be feared, the possibility should be borne in mind if fall in blood sugar, shock, and so on suddenly occur in patients treated with massive prednisone doses. This applies especially if the patient's salt intake is simultaneously reduced. In stress situations patients with secondary insufficiency of the adrenal cortex as the result of long-continued prednisone treatment should receive the addition of cortisone or hydrocortisone.

Pancytopenia and Granulocytopenia After Carbutamide in Diabetes. S. Aarseth and H. Willumsen. Nord. med. 59:564-565 (April 17) 1958 (In Norwegian) [Stockholm].

Three cases of hemorrhagic complications on carbutamide treatment are reported, 2 with fatal outcome. Diabetes mellitus developed in a man, aged 81 years, who had previously been well. Carbutamide was given in the usual therapeutic doses of 28 and 13 Gm., with an interval of 6 months. There was progressive bone marrow depression, with anemia, thrombocytopenia, and total disappearance of white blood corpuscles. Death occurred 12 days after the carbutamide was withdrawn. In the second case, in a woman, aged 70, with long-continued heart disease and recently diagnosed diabetes mellitus, polyclinical treatment with carbutamide in the usual doses was effective in reducing the blood sugar. After 4 weeks general dermatitis and fever set in, with almost total disappearance of neutrophil granulocytes. The patient died. The total carbutamide dose was 43 Gm. in 7 weeks. The third patient, a man, aged 68, with moderate diabetes of 3 years' standing, was treated with a total of 30 Gm. of carbutamide in the course of 4 weeks. Because of fever and diarrhea the treatment was discontinued; another not readily resorbable sulfonamide was given for a couple of days. Examination of the blood showed anemia and complete granulocytopenia. The patient recovered after massive doses of penicillin and blood transfusions. Carbutamide involves a not inconsiderable risk of hematological complications threatening life, especially granulocytopenia. Since similar complications have not been observed on tolbutamide treatment, and since the effect in reduction of blood sugar is the same as that of carbutamide, carbutamide therapy should not be employed in the treatment of diabetes.

PATHOLOGY

The Spread of Lung Cancer to the Brain. W. I. B. Onuigbo. Brit. J. Tuberc. 52:141-148 (April) 1958 [London].

It is a striking feature of lung cancer that brain and adrenal metastases frequently coexist. In a previous paper the author had demonstrated that the topographic distribution of adrenal deposits accords well with lymph-borne and not artery-borne metastasis. This finding posed the question of whether a similar pattern was demonstrable in the case of brain secondaries. Because it has been denied that the brain has lymphatic connections, the current view is that lung cancer metastasizes to this organ via the arteries. Theoretically, arterial scattering of tumor emboli should result in an even distribution of deposits on either side of the brain. Lymphogenous dissemination to the brain, however, would lead to ipsilateral preponderance of deposits. The author reviewed cases of bronchial carcinoma from the autopsy records of the Scottish Medical Schools and the Stobhill General Hospital, Glasgow. In every case showing unilateral metastases in the cerebral or cerebellar hemisphere, it was noted whether the deposits were ipsilateral or contralateral. For bilateral metastases, the side containing the larger deposits was similarly noted.

Two hundred fifty cases fulfilling these criteria were analyzed. Of 177 patients showing unilateral deposits, 100 were ipsilateral and 77 were contralateral; of 73 patients showing bilateral growths, 43 contained the larger deposits ipsilaterally and 30 did so contralaterally. Thus, in the whole series of 250 cases, ipsilateral tendency was exhibited on 143 occasions, and the contralateral trend was manifest 107 times. This finding is statistically significant and is in keeping with lymphatic metastasis. Fifty-five cases collected from the literature also exhibited a statistically significant ipsilateral preponderance. Other factors indicating that the spread of lung cancer to the brain takes place by way of the lymphatics, rather than the arteries, are as follows: 1. Subdiaphragmatic tumors metastasize to the brain more often than do infradiaphragmatic tumors. 2. The relatively nearer cerebellum is a site of metastatic predilection. 3. The outstanding histopathological features of brain metastases include the common finding of tumor cells in perivascular spaces and the difficulty of demonstrating them inside vessels. Two controversial questions are asked. First, do lymphatics effect connections with these perivascular spaces? Many anatomists thought so. Secondly, are the subarachnoid spaces and the lymphatic system connected? Indian ink introduced into the cranial subarachnoid appeared within 4 hours in cervical nodes and ultimately in intrathoracic nodes.

Rheumatic Fever and Rheumatic Heart Disease: II. Life Expectation and Natural History. E. Waaler. Acta med. scandinav. 160:293-303 (No. 4) 1958 (In English) [Stockholm].

The authors report on 211 patients who died at the University Hospital in Bergen, Norway, between 1941 and 1955 and in whom a diagnosis of rheumatic heart disease was made on autopsy. History revealed rheumatic fever in 46 (60%) of the 76 men and in 61 (45%) of the 135 women. This higher incidence of rheumatic fever in men, as compared with women, was not apparent in the younger age groups, but it was significant in the older age groups. Chronic valvular disease was recorded as the cause of death in patients whose average age was 52 or 53 years at the time of death. Death occurred at an earlier age in patients with bacterial endocarditis than in those with pure rheumatic lesions. The average interval between the first attack of rheumatic fever and death was 30 to 32 years in patients dying of chronic valvular disease. The mean age at death was strikingly higher in these patients than in those whose cases were collected from the United States literature. It seems that rheumatic fever and rheumatic heart disease have had a milder course in Norway than in the northeastern part of the United States. The difference may be partly due to the fact that the patients in Norway were less selected, but it must also be remembered that rheumatic heart disease in more recent years has had a tendency to run a milder course than in the years between 1900 and 1920, the period with which the American studies were concerned.

Acute rheumatic fever occurs mainly in children and adolescents. A severe valvular lesion is more likely to occur in patients with rheumatic heart disease and a positive history of rheumatic fever than in those with a negative history of rheumatic fever. Rheumatic heart disease acquired in childhood and adolescence takes a more severe course than that starting in adult life. The findings in the 135 women also indicated that in adult life the silent insidious types of rheumatic heart disease are particularly common in women. The preponderance of women among the 211 patients is partly due to the fact that women are apparently more susceptible to the hyperergic inflammatory type of reaction than men. Microscopic evidence of active rheumatic inflammation was found in only 5 men and 9 women with chronic disease, but the small number of patients does not permit any conclusions concerning a possible difference between men and women. This low incidence of activity on microscopic examination is probably partly due to the fact that 34 of 92 patients who died of chronic valvular disease were above 60 years of age. The longest interval between clinical signs of activity and microscopic findings of activity was 35 years. The clinical ability to make a diagnosis of activity of rheumatic heart disease seems to be lacking, and inflammatory scarring of the valves may take place without being revealed by definite clinical signs.

Presence of Neoplastic Cells in the Peripheral Arterial Blood of Patients with Bronchial Cancer. C. Colombo, G. Maggi and F. Rolfo. Minerva med. 49:725-730 (Feb. 28) 1958 (In Italian) [Turin, Italy].

Peripheral arterial blood of 13 patients with bronchial cancer was investigated for possible presence of neoplastic cells. Specimens of 5 cc. of serum were obtained from the femoral arteries before the surgical operations. Tumor cells were found in the serum of 2 patients. The first patient was a 56-year-old man who had a squamous tumor in the right main bronchus, with diffusion in the carina and metastases in the hilar lymph nodes during a period of 8 months. Sixteen tumor cells were found in his peripheral blood. After he underwent pneumonectomy, histological examination revealed malignant infiltration of the wall of a large thrombotic vein, with invasion of tumor cells into the vessel's lumen. The second patient was a 59-year-old man who had a tumor in the upper part of the left bronchus, which could not be reached by forceps. Bone metastases were roentgenologically visible. Five tumor cells were counted in the peripheral blood. Tumor cells in the peripheral arterial blood of these patients were 2 to 4 times larger than neutrophils and were round or egg-shaped. They had a large cytoplasm clearly outlined, were slightly eosinophilic, and had no granulation. Nuclei were large, some of them vesical, with spots of chromatin which were arranged irregularly. Nucleoli were identifiable and in some instances well marked.

BOOK REVIEWS

Rehabilitation of the Cardiovascular Patient. By Paul Dudley White, M.D., Howard A. Rusk, M.D., Professor and Chairman, Department of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, New York, Philip R. Lee, M.D., and Bryan Williams, M.D., Clinical Instructor in Medicine, University of Texas, Southwestern Medical School, Dallas. Cloth. $7. Pp. 176, with 31 illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1958.

With the control of acute infectious diseases and the longer life span, chronic degenerative disease of which cardiovascular disease is the most important becomes a major problem not only medically but sociologically. This book shows how patients who have suffered a myocardial infarction or hemiplegia or who have rheumatic heart disease can be rehabilitated and made useful happy citizens. Although the rehabilitation of the cardiac patient has received attention only within the past 10 to 15 years, enormous strides have been made and the techniques described in this book have produced results in many patients who would have ordinarily been consigned to hopeless invalidism. The patient with hemiplegia can also be helped materially, and this book shows how. This small volume should be in every physician's library for ready reference.

On the Utility of Medical History. Iago Galdston, M.D., editor. Monograph I, Institute on Social and Historical Medicine, New York Academy of Medicine. Cloth. $2. Pp. 73. International Universities Press, Inc., 227 W. 13th St., New York 11, 1957.

This volume is the first of a new series of monographs published by the Institute on Social and Historical Medicine. The purpose of this organization is "to inquire whether medical history can in effect serve to illuminate current problems and issues in medicine. Can they, when seen in the perspective of historical data and historical derivations, be better understood? Can the knowledge of past experiences, historically comprehended, sharpen judgment as to the values and the probable effectiveness of proposed actions?" The book could well have been subtitled, *Apologia pro historia medicinae.* Many pages are devoted to justify the serious study of medical history in the face of a widespread apathy on the part of the medical profession. Thus, for example, Ackerknecht describes the state of medical history courses in medical schools while Schrecker defends the position that we can learn something from history by showing the mutually beneficial relationship existing between the systematic and the historical approach to an area of knowledge. Temkin inquires into the nature of medical historiography, and Zilboorg presents a brief analysis of "the emotional changes of the period that do not permit people to investigate things properly." The practicing physician, the medical student, and others professionally concerned with medicine who read this book should take with them the realization that something good may be said for medical history.

Textbook of Gynecology. By John I. Brewer, B.S., M.D., Ph.D., Professor of Obstetrics and Gynecology, Northwestern University Medical School, Chicago. Second edition. Cloth. $15. Pp. 742, with 204 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

This edition, like the first, is designed for use by undergraduate students "to prepare them for the general practice of medicine." Details are reduced to a minimum, although one gets the impression that the author's enthusiasm overcomes his reticence at times. There has been extensive revision of the first edition. An excellent chapter on endocrinology has been added by DeCosta. This describes in some detail the sex abnormalities of development in a clear and authoritative manner. This new edition repeats the division into two parts. In the first, the whole of gynecology is approached from the point of view of symptoms. In the second, the field is re-covered on the basis of organs and their diseases, in so far as possible. The author recognizes that this leads to some repetition. It also makes for a scattering of information throughout the book and probably for reduction of details because of space limitations. This is an excellent approach in talking to students but leaves something to be desired in the use of the book for reference. The book is printed on attractive paper which magnificently shows up the multiple photomicrographs and other illustrations. Typographical errors have been held to a minimum, and a useful index is appended. This is an excellent introduction to gynecology for the undergraduate.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

EXAMINATIONS FOR SCHOOL CHILDREN

To the Editor:—*In a fairly well-to-do suburb, private physicians are requested to include in physical examinations for elementary school children a tuberculin patch test, hemoglobin level estimation, and urinalysis for all, including those who are apparently healthy and asymptomatic. Opinions as to the needs and merits are divided. Please comment on this practice.*

H. H. Neumann, M.D., Elmont, N. Y.

Answer.—The tuberculin test is highly recommended as a periodic procedure for all children after the age of two months and for as long as no reaction is elicited. This is the earliest method by which tuberculosis can be diagnosed. It is important to detect this disease, if it occurs, as early as possible in the child's body. Since 1912 it has been known that the child who reacts to tuberculin has tuberculous lesions. Ghon established this fact by meticulous postmortem examinations of the bodies of 184 children who during life had no evidence of tuberculosis except the tuberculin reaction. He found lesions in 183; the body of the remaining child was not completely examined. While these lesions are usually too small to be detected by physical examination, including inspection of the chest by x-ray film, they are nevertheless potential sources of gross clinical disease. A child who becomes a reactor to tuberculin has been in close contact usually with an adult, such as a parent, grandparent, or someone else who has contagious disease. Seeking the source of the infection among adult associates is a most valuable clinical case-finding method. Obviously, the earlier the infection in the child is found, the better are the results for the child. Moreover, the earlier the responsible case is detected, the fewer other persons will be infected and the better the individual's chance of recovery will be. With the advent of antituberculosis drugs, the importance of finding the diseased child soon after the infection has occurred is increased. A great many recent tuberculin converters are now being treated with these drugs. Those currently available apparently are not germicidal, but they suppress tubercle bacilli. Although they do not cure, there is some evidence that they may occasionally prevent the development of acute forms, such as miliary disease or meningitis. If a germicidal drug becomes available the importance of finding the infection early is obvious. Then the lesions are microscopic and vascular; the drug may be expected to enter so as to come in contact with all tubercle bacilli. However, as time passes tuberculous lesions often lose their blood supply, after which a drug could not be expected to reach the organism in avascular necrotic tissue. In most parts of the United States, the number of children who develop tuberculosis so as to become reactors to tuberculin is quite small, often not more than 2 or 3% during the grade-school period, and in some places none do so. Control of tuberculosis among the cattle herds, isolation of persons in sanatoriums, and treatment of others has so reduced the populations of both the human and bovine types of tubercle bacilli that the situation is in sharp contrast with that of a few decades ago, when so many became infected during the period of childhood. There is a high incidence of tuberculosis among persons 40 years of age or older, as manifested by the tuberculin reaction. Some of these older persons become contagious unknowingly and disseminate tubercle bacilli to children. In addition to keeping all older tuberculin reactors under periodic examination, children everywhere should be tested periodically to make certain that those who may be infected from unsuspected sources are detected promptly. Urinalysis and hemoglobin level estimation are important routine procedures, but they do not have the significance that the tuberculin test has with reference to schools and communities.

VISION SCREENING IN SCHOOLS

To the Editor:—*Please supply some information on the current methods for visual screening examinations in school children. What should the standard procedure be, and by whom should the children be examined at the school?*

S. Henry Thaler, M.D., Huntington, N. Y.

Answer.—The Joint Committee on Health Problems in Education of the National Education Association and the American Medical Association has made definite suggestions on vision screening in schools in its second edition of "Health Appraisal of School Children" as follows: "Emphasis must be placed on the fact that school tests for visual acuity are screening tests and are not intended to diagnose the nature of eye defects. They reveal that a child does not see well, but the presence or absence of visual defects requiring correction cannot be determined entirely on the basis of screening tests.

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

Screening tests should, therefore, be the province of teachers, nurses, or technologists and not of eye physicians. The most commonly used visual screening procedure is to test with the Snellen chart, at 20 feet under proper lighting, or with the Massachusetts Vision Test based upon the Snellen chart." The details of the testing procedure, including preparation of pupils, arrangement of room and equipment, and referral of children for eye examination, are given in "Health Appraisal of School Children," which may be obtained from the Bureau of Health Education of the American Medical Association. This booklet provides information relating to other common screening tests used in the school health program.

CHRONIC CYSTIC MASTITIS AND CONTRACEPTION

To the Editor:—*Several years ago in* The Journal, *Dec. 30, 1950, page 1602, in the Queries and Minor Notes section, it was stated in answer to a question that the use of a diaphragm for contraceptive purposes was inadvisable in the presence of chronic cystic mastitis because resultant ovarian stimulation might cause cancer. Would this opinion be rephrased in the light of present evidence?* *M.D., Missouri.*

Answer.—The answer to this question remains the same for the following reasons. In experimental animals it has been shown that estrogens possess carcinogenic activity, giving rise to tumors of the breast and uterine cervix. It has been known for some time that the female breast undergoes cyclic changes in response to ovarian hormones (Rosenburg, *Virhow's Arch. f. Path. Anat.* 261:256, 1925). Chronic cystic mastitis (microscopically diagnosed) is due to unopposed estrogen effect or poor lutein secretion and is treated by progesterone (Womack, personal communication; Geschickter, Diseases of Breast, Philadelphia, J. B. Lippincott Company, 1943). Evidence presented by Geschickter (p. 237) implies that chronic cystic mastitis is hormonal in origin and that the disease occurs only when the cyclic changes are present. It is not found in the male breast or during adolescence or pregnancy. According to Cheatle and Cutler (Tumors of Breast, London, Edward Arnold & Co., 1931), approximately 20% of all mammary cancers have their onset in the changes of chronic cystic mastitis. Warren (*Surg. Gynec. & Obst.* 71:257, 1940) has confirmed this observation. Sommers and Lombard (*A. M. A. Arch. Path.* 56:462, 1953) found that 87% of women who died of cancer of the breast had hyperplastic ovarian cortical stroma at autopsy. Both ovaries and adrenals were normal or atrophic in less than 3% of cancer cases. Endometrium and uninvolved breast epithelium were also frequently hyperplastic, accompanying breast cancer. The few cervical specimens available usually showed estrogen effects even in the postmenopause cancer cases. Synthesis of the observations supported the idea of presence of a prolonged estrogenic stimulation of endometrium and breast in the background of about two-thirds of the breast cases. Either ovarian stroma or adrenal cortex, or both, were thought to produce the estrogen, which was concluded to be as important in the development of the human breast cancer as has been shown in rodent mammary cancer (Sommers, *Lab. Invest.* 4:160, 1955). Prevention of conception (not by diaphragm alone) may extend the prolonged estrogen effect and thus, in a susceptible individual, increase the risk of breast or cervix cancer. Sexual stimulation not resulting in pregnancy for long periods increases the incidence of functional disturbances of the female genital tract, namely, cervicitis, abnormal bleeding, and pelvic congestion. In studies of cervical tissue associated with carcinoma in situ in the same patient, it appears that basal cell hyperactivity, atypia, and epidermidalization are increased in these patients. Therefore, one concludes that contraception is not wise in patients affected with cystic mastitis. Pregnancy would be good therapy. It is not meant to intimate that a diaphragm has any direct affect on the cervix. The contention is, from evidence submitted, that preventing pregnancy has the deleterious effect.

Answer.—There is not sufficient evidence to indicate that a diaphragm pessary could indirectly influence preexisting chronic cystic mastitis. Even though the incidence of malignancy of the breast may be somewhat higher in those patients in whom chronic cystic mastitis has been present, the use of a diaphragm pessary seems rather far removed as a possible causal agent. Issue on this point is more in the realm of polemics than in that of deduction from factual data.

BOWEL IRREGULARITY

To the Editor:—*A woman, 69 years old, has suffered from chronic constipation since she was a small girl. She was then given epsom salt, and later she used a variety of such cathartics as mineral oil, cascara, and phenolphthalein. Recently she has taken a sodium phosphate laxative every three days. Now, aside from the constipation, she does not have a formed stool but water is always present with much gas. She is well nourished, in good physical condition, and not overweight. What could be suggested in way of a diet for this woman? How can the cathartic habit be stopped?*

Burton G. McGarry, M.D., Sarasota, Fla.

Answer.—Until proved otherwise, bowel irregularity indicates cancer of the rectum or distal colon, whether there is a past history of cathartic abuse or not. It is therefore assumed that this woman has had a thorough investigation of the large intestine, including rectal examination, proctosigmoidoscopy, and barium enema, and that findings in these studies were negative. She has to be weaned from her purgatives and enemas. To achieve this, it will be necessary to brainwash her on the subject of bowel habits along the line that the old belief in intestinal toxemia from chronic constipation is no longer tenable but that it will be necessary to prevent mechanical damage to the rectum and anal sphincter by inspissated feces. The diet will need supervision, and attention must be given to adequate consumption of water and roughage. All purgatives and enemas should be withdrawn. The stool should be prevented from becoming hard and impacted. Mineral oil emulsion is somewhat out of favor at present because of its interference with vitamin absorption, but, used carefully and for short periods of time in an alert patient who has no difficulty in swallowing, it is still of great value. At first, one tablespoonful nightly can be given and, later, one tablespoonful at bedtime if no bowel movement has occurred on that day. With the addition of a water-retaining substance, such as agar-agar, psyllium seed, or methylcellulose, the amount of mineral oil can be decreased. At start of therapy the bowel movements will doubtless be irregular, but, with the help of an occasional enema and dose of cascara sagrada, this difficulty will be overcome; these should only be taken by order of the physician. The essential point, however, will be to convince the patient that a daily bowel movement is not essential for health, that she can go without one for days without ill effect, and that if she follows instructions normal colonic peristalsis will return, even at her age.

ANTIBIOTICS AND LONGEVITY

To the Editor:—*It has been stated that the greatest factor in longevity is heredity. Have the antibiotic drugs changed this viewpoint or materially contributed toward longevity as such?*

Jules Magnette, M.D., Reno, Nev.

Answer.—Since the antibiotics have been in general use for little more than half of a single generation, the answer to this question must be based on speculation and analogy. They will probably pull through childhood a number of individuals who have inherently weak constitutions and who will not live out the normal span of adult life. Ploetz' study of the infant mortality in the royal and princely families of Europe, where every child has had the advantage of the best care that the state of science at the time of his birth could furnish, showed a close relation between the length of the father's life and the child's mortality. If the parents were short-lived, the child evidently inherited the same weak constitution and his own expectation of life was not so good. This survival of inherently weak children who will not live to advanced age will tend, to some extent, at least, to counterbalance the prolongation of life of elderly persons through a lower death rate from pneumonia and other familiar causes. At present, an "educated guess" might be that the antibiotics will lengthen the lives of some individuals, because of their effect on the infectious diseases, that they will not be of much effect on the degenerative diseases, in which the influence of heredity is more important, and that the net result may be very little change in the average longevity of the race.

STEROID MEDICATION AND RHEUMATIC FEVER

To the Editor:—*An 8-year-old girl with rheumatic fever was treated with a large dosage of aspirin and 15 mg. of prednisolone daily. She has also received 200,000 units of penicillin daily, by mouth. Fever and swollen and painful joints subsided with this therapy. After consultation the prednisone was gradually withdrawn, but then the symptoms reappeared. The patient has been hospitalized twice for blood, electrocardiographic, and chest examinations. So far, there are no cardiac symptoms. The present medication includes large dosages of aspirin plus 5 mg. of prednisolone daily. This treatment keeps her symptoms only partially checked. She has always shown marked improvement after the prednisolone is administered. Should a maintenance dosage of prednisolone be continued, or should this drug be withdrawn? Please give suggestions for treatment.*

M.D., Virginia.

Answer.—The use of steroids in the treatment of acute rheumatic fever, according to most workers in the field, depends on whether carditis is present. If polyarthritis is the only major manifestation and if evidence of a beta-hemolytic streptococcic infection suggests that the disease is acute rheumatic fever rather than rheumatoid arthritis, lupus erythematosus, or other diseases associated with polyarthritis, the first therapeutic measure taken in addition to bed rest is eradication of the Streptococcus. Adequate doses of penicillin are given for 10 days, preferably parenterally, according to the dosage schedules recommended by the American Heart Association. Thereafter, the patient is maintained on prophylactic medication according to the AHA-recommended regimens (1,200,000 units of benzathine penicillin G given intramuscularly every four weeks, or 250,000 units of penicillin G given orally twice daily, or 0.5 Gm. of sulfadiazine given twice daily). Repeated throat cultures should then be negative for beta-hemolytic streptococci. Symptomatic relief is afforded by the use of salycilates, starting with a dose of 1 grain (0.06 Gm.) per pound of body weight in

24 hours (in divided doses) for the first two days (150-grain [9.72-Gm.] maximum daily dose), then ⅔ grain per pound of body weight in 24 hours for five days, and finally ½ grain per pound of body weight in 24 hours for the duration of therapy. Therapy is continued for several weeks after all physical and laboratory findings (such as erythrocyte sedimentation rate, white blood cell count, and C-reactive protein precipitation) of activity of the rheumatic process return to normal values. In the usual case this entails a six-week period of therapy. Steroids are usually not used unless carditis is present. In addition to therapy for symptomatic relief, a high-vitamin, high-protein diet is recommended. The patient is kept at bed rest until therapy with salycilates has been discontinued and all signs of the rheumatic process have returned to normal. He is then allowed increasing activity, and, if in two to three weeks no signs of rheumatic disease become evident, he is allowed full, unrestricted activity, provided carditis was not manifest. The recurrence of joint manifestations in acute rheumatic fever is not uncommon if suppressive therapy (salycilates or steroids) is discontinued too early. However, a six-week course of therapy followed by reappearance of polyarthritis without evidence of carditis on discontinuing therapy suggests the possibility that the disease is other than rheumatic fever, unless evidence of reinfection with beta-hemolytic streptococci is obtained.

WEIGHT REDUCTION BY COATING THE FOOD

To the Editor:—*Is there any method of lowering the calorie value of ingested food by reducing the dietary efficiency of the gastrointestinal tract? Could this be done by means of some oral medication that would coat the food particles and prevent complete action on them by the digestive fluids or act in some similar manner? It would seem that such a method would be an excellent way to obtain weight reduction in individuals not willing to restrain their dietary intake. A vitamin-mineral supplement could be given between meals to prevent deficiency developing from the medical or chemical absorption-hindering agent.*

J. D. Marshall, M.D., Portland, Ore.

Answer.—To the knowledge of this consultant, a method of weight reduction by coating the food has never been publicized. Mineral oil is the only such substance that comes immediately to mind as being indigestible. The Food and Drug Administration does not permit it in foods, however. Such a method leaves quite a bit to be desired. While it may effect a reduction in weight, no effort is being made to retrain the person in his eating habits. This latter aspect is particularly important if the person is to maintain whatever weight loss is achieved. He certainly will not maintain it by continuing to eat in an accustomed manner. It is seriously questioned whether the continued ingestion of a "coated" diet would be physiologically desirable.

MORPHEA OF THE SCALP

To the Editor:—*The mother of a 4-year-old boy who has morphea of the scalp wishes to know whether the condition will be permanent, what treatment will halt the progress of the disease, and whether the disease should be allowed to take its course. The lesion occupies an area of about 1 by 2 in. in the middle of the scalp.*

Edwin L. Stickney, M.D., Broadus, Mont.

Answer.—The course of morphea, or circumscribed scleroderma, either is chronic, and as such may run a course of 1 to 10 years, or is, occasionally, subacute, and lasts a comparatively short time. As the disease clears up, there is commonly left a thin, inconspicuous, atrophic area. This lesion may be even less conspicuous in the scalp, although the alopecia of the site will probably be permanent. One must be certain that the disease is morphea rather than a congenital defect of the scalp (Behrman, The Scalp in Health and Disease, St. Louis, C. V. Mosby Company, 1952). There is no specific treatment of value for circumscribed scleroderma, although various measures have been recommended. These include massage, bland ointments containing 1% pilocarpine, acetylcholine chloride administered by iontophoresis, and other forms of vasodilatation. In view of the particular location described, the employment of gentle massage and the application of a mild vasodilating type of ointment may be of some small benefit.

PULLING HAIR OUT OF THE HEAD

To the Editor:—*A 2-year-old girl has been pulling hair out of her head for the past several months. Hair is missing from practically the entire back of her head. Please give suggestions on cause and cure.*

Robert M. Stansbury, M.D., Lancaster, Calif.

Answer.—It is assumed that the evidence is definite that the child is pulling out the hair and that this is not a bald area which results from the child's lying excessively in the supine position (as might occur in a severely neglected or retarded child). One would be concerned about emotional factors in the etiology of the symptom described. It could be assumed that for some reason the child's gratification from her relationships with parents and others is insufficient and that she is, in consequence, becoming more preoccupied with her body. There is no specific psychodynamic constellation which produces this symptom. In a child of this age, however, one would be concerned about any recent separation from parents or grandparents, the recent birth of a sibling, excessive pressures in toilet training or feeding, or any other psychologically upsetting circumstance. Any one of these —or a grouping of them—may be present, and treatment should be directed at minimizing these factors while providing gratifying play experiences for the child.

MICRO-ORGANISMS IN TOBACCO

To the Editor:—*Has there been any investigation of the type of micro-organisms found in the tobacco of cigarettes and of whether these are a source of infection to the respiratory system, the gastrointestinal tract, or other systems?*

M.D., New York.

Answer.—There is an abundant flora of micro-organisms in the tobacco leaf (Frankenburg, *Advances Enzymol.* 6:309, 1946; **10**:325, 1950) as in most organic material. There is no record in the literature of any that are harmful to man or other animal species. The process of combustion would destroy any living organisms in smoked tobacco. Among the number of references to the bactericidal effects of tobacco smoke are reports by the following workers: Appleton and Lehmer (*Dental Cosmos* **70**:1111, 1928), Miller (*Independ. Pract.* 5:284, 1884), Parfentjev, reported by Hammond (*Cancer* 7:1100, 1954), Tassinari (*Centralbl. f. Bakteriol. u. Parasitenk.* 4:449, 1888), and Turkheim (*J. Dent. Res.* **31**:326, 1952).

STERILIZATION OF SIGMOIDOSCOPES

To the Editor:—*Should sigmoidoscopes be sterilized between patients, or is washing with soap and water adequate? If sterilization is necessary, would any germicidal liquid agent be considered sufficient?* *M.D., Louisiana.*

Answer.—Sigmoidoscopes should be sterilized before they are utilized for the purpose of examining the terminal portion of the colon. Sterilization is accomplished best by immersing the instrument in boiling water.

VITAMIN E FOR "HOT FLASHES"

To the Editor:—*In January, 1958, a 42-year-old woman had a total hysterectomy and bilateral salpingo-oophorectomy. There was an ovarian cyst on the right side which contained an adenocarcinoma, grade 2. She received 30 deep x-ray treatments. Is there any medication, under the circumstances, which could be given to alleviate the intensity of "hot flashes"?*

C. E. Cassaday, M.D., Mt. Vernon, Ohio.

Answer.—The use of alpha tocopherol (vitamin E), 25 mg. given three times a day, is recommended. Estrogens are definitely contraindicated in individuals who have been treated for carcinoma, due to the fact that they may activate dormant cells to malignant phases. Alpha tocopherol causes no such stimulation of dormant cells which may have this propensity. This consultant has had some success with this medication; it is recommended with the belief that it has definite value in diminishing or causing absence of hot flashes.

NEOSTIGMINE FOR A PREGNANCY TEST

To the Editor:—*Please advise as to the current status of the use of neostigmine methylsulfate as a pregnancy screening test. Have there been any reports of its use precipitating miscarriages?*

M.D., Massachusetts.

Answer.—The administration of neostigmine methylsulfate (1:2,000) daily for three consecutive days will usually be followed by uterine bleeding within three days if the patient is not pregnant. This procedure applies only to delayed menstruation in women who have had a normal menstrual history up to the last period. It does not apply either to early or to prolonged amenorrhea due to endocrine dysfunction or to local organic changes. There is no evidence that this drug precipitates miscarriages.

CLEANING EYE GLASSES

To the Editor:—*What is the best way to clean eye glasses? Please comment on the silicone treated papers, "special" cleaning fluids, and plain soap and water.* *M.D., California.*

Answer.—Silicone treated papers are not usually recommended for general use, since silicone itself will remove any nonreflective coatings that may have been applied to the lenses. No harm can come to any lenses from this paper, however, if they have not been so coated. Soap and water continues to be an excellent cleaner, provided a mild hand soap is used. Stronger soaps might affect some of the trims that are often applied to women's frames. Several good cleaning fluids, available in any optical office, also do an excellent job of cleaning. These contain a mild alcohol solution, which takes off most spots and dirt.

PREVENTING BLOOD COAGULATION

To the Editor:—*How many units (on the average) of heparin are required per 100 ml. of whole blood to prevent coagulation?*

M.D., New York.

Answer.—The usual amount of a commercial preparation of heparin used to prevent the coagulation of collected blood in glass is 4 mg. per 100 ml. (1 mg. is equal to 10 units). If blood is collected in a plastic or silicone-coated container, a smaller amount will be needed to keep the blood noncoagulable.

WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

HEW Study on Aging Directed by House . .

Forand Plan Omitted from Social Security Amendments . .

Jenkins-Keogh Bill Passes House . .

COMMITTEE CALLS FOR STUDY OF PROBLEMS OF HEALTH CARE OF AGED

As an outgrowth of its hearings on the Forand bill and other social security proposals, the House Ways and Means Committee is calling on Secretary Folsom for a study of the various possibilities for financing the health care of the aged. A report must be completed by next Feb.1.

In reporting out a bill with changes in the social security act (see following story) the committee did nothing about Rep. Aime J. Forand's proposal for the hospitalization of social security beneficiaries and their dependents. But it did recognize the problem by requesting the Department of Health, Education, and Welfare to complete an investigation and report back with recommendations so Congress will be in a better position to decide what legislative measures, if any, should then be taken to meet the problem.

The committee is particularly interested in having the HEW study explore the possibility of adding to social security taxes and using the money to buy "private or nonprofit" health insurance which would take effect upon ordinary retirement at age 65 or retirement for disability at age 50.

At hearings, the American Hospital Association had proposed a similar study of the problem of the health care of the aged but by an advisory committee that would be created by the Ways and Means Committee and report back to that committee.

The AFL-CIO, a principal sponsor of the Forand measure, was quick to respond to the committee's decision not to act on that hospitalization measure at this time. AFL-CIO President George Meany said in a statement that this "cannot be construed as a decision of the Congress to discard this proposal . . . it is by no means a dead issue." Mr. Meany's statement added: "The Forand proposal will be a live issue as long as the problem remains unsolved, and we intend to urge the adoption of the Forand proposal along with other measures further to improve the system as soon as the 86th Congress convenes next January."

The Ways and Means report notes that the committee "is very much aware" of the problems faced by the aging in paying for hospital and nursing home services and that a number of bills were introduced on this subject, including the Forand bill for hospitalization. The report recalls that "considerable testimony" was devoted to pointing out that presently insurance against the costs of needed hospital and nursing home services is out of reach of many older people and "there appears to be a need for making this protection available. . . ." But the report then declares:

"Your committee believes, however, that more information on the practicability and the costs of providing this kind of protection through various methods should be available before it entertains any recommendation for legislation on the subject. A study of alternative ways of providing insurance against the cost of hospital and nursing home care for old-age, survivors, and disability insurance beneficiaries should be made.

"The alternatives explored should include among other proposals: a prepayment plan under which persons would, during their working years, pay additional social security contributions which would be used to buy this type of insurance (to take effect when the individual becomes an old-age, survivors, and disability insurance beneficiary) from private and nonprofit health insurance organizations; other methods of providing insurance against the cost of hospital and nursing home care under title II; and any other method which offers reasonable prospects for protecting old-age, survivors, and disability insurance beneficiaries against the cost of needed hospital and nursing home care. The study would include, for each of the several alternatives, an evaluation of (1) cost of the benefits and (2) administrative implications.

"Your committee has asked the Secretary of Health, Education, and Welfare to conduct such a study and to report the results on or before Feb. 1, 1959. With the results of such a study available, the Congress will be in a better position to decide what legislative measures, if any, should then be taken to meet the problem."

SOCIAL SECURITY BILL OMITS FORAND HOSPITALIZATION PLAN

An omnibus social security bill amending the 22-year-old act has passed the House. It awaits an uncertain fate in the Senate because of the expected rush for adjournment. The measure is distinctive both for the things it proposes and the things it leaves out. The controversial free federal hospitalization and surgical plan proposed by Rep. Aime Forand (D., R. I.) is not included in the bill, nor is the inclusion of physicians under the social security system proposed.

(Continued on next page)

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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The bill increases monthly social security benefits by 7%, with a $3 minimum increase. The taxable wage base is raised from $4,200 to $4,800, and the actual withholding tax on employer and employe is increased 0.25% each, while the self-employed tax goes up 0.375%. Additional increases in taxes are proposed every three years until by 1969 the self-employed rate would be 6.75% of gross earnings. The present rate is 3.375%.

Chairman Wilbur Mills (D., Ark.) said in a statement that one of the primary considerations of the committee was that of "substantially improving the actuarial soundness of the social security system. The increased revenues provided under the bill are more than adequate to finance the benefit increases."

Other proposed changes in the law would provide benefits for dependents of disabled workers who are now eligible for social security at age 50. This would make the disabled worker and his family eligible for monthly payments up to $254. The maximum for a disabled worker now is $108.50 with no dependents benefits. Also, the bill would (1) provide for paying disability benefits for as much as 12 months before the month in which an application is filed and (2) postpone for three years the June 30, 1958, deadline for filing fully retroactive applications for freezing a disabled person's benefit status.

Under the committee bill, the state would have complete flexibility in using federal funds for the financing of medical care of the aged, the blind, and the disabled and dependent children. Under the bill, the state would receive a portion of $66 times the number of adult assistance recipients, and from this pool it could meet all payments, subsistence or medical. Under present law, the federal government contributes up to a maximum of $60 for the basic needs, which in a few cases includes direct medical care payments to the individual. In addition, it provides up to $3 each for the medical care of adults and $1.50 each for children, to be matched 50-50 by the states. But the latter funds must be used for vendor payments—to the doctor, the hospital, nurse or pharmacist.

Under the bill, the state could take advantage of all government money offered for subsistence and medical care and expend the money in any way it saw fit. Furthermore, the money would come in a lump-sum, statewide allotment, all of which could be used to pay the small and the large hospital bills. There would be no distinction between cash payments to the individual—recipient payments—and vendor payments, which the state pays directly to surveyors of medical care.

KEOGH BILL PASSES HOUSE; DECISION NOW RESTS WITH SENATE

What action the Senate takes—or doesn't take—in the closing days of the session, possibly the closing hours, will determine the fate of the Keogh bill to permit the self-employed to defer income taxes on money paid into retirement funds.

After being reported out of the Ways and Means Committee on a split vote, the bill went through the House without a record vote. However, Rep. John Byrnes (R., Wis.) criticized it, pointing out that it would involve loss of tax money at a time the government is increasing the national debt.

At this writing there are three possibilities for action:

1. Senate passage and enactment of the Keogh bill. In this case the measure would have to overcome admitted opposition in the Senate Finance Committee.

2. Passage by the Senate of an aid-to-small business bill that has a section authorizing a different form of tax deferment (limit $1,000 annually) for employed not covered by company pension plans as well as the self-employed. This then would go to conference with the House, which has passed its own small business bill, but without a tax deferral section.

3. Amendment of the Senate small business bill to substitute the Keogh plan for the more limited Senate proposal, which probably wouldn't be acceptable to Sen. John Sparkman (D., Ala.), sponsor of the small business bill.

The Keogh bill would allow the self-employed to set aside up to $2,500 per year, or $50,000 for a lifetime, with income taxes to be paid when the money is recovered in the form of annuity benefits.

VETERANS ADMINISTRATION

Dr. George E. Armstrong, vice-president for medical affairs of New York University and director of Bellevue Medical Center, has been elected chairman of the VA special medical advisory group. He is being succeeded as vice-chairman by Dr. H. P. Rome of Rochester, Minn. Dr. Robert M. Zollinger's two-year term as chairman expired June 30.

A VA survey shows that nearly half of the 2,000 war-blinded veterans of World War II and the Korean war hold jobs, even though many have other physical handicaps.

Dr. Benjamin B. Wells, head of professional services at the New Orleans hospital, has been appointed director of VA medical education services in Washington.

Dr. Edward Dunner is the new chief of clinical studies of the VA in Washington. Since 1955 he has been secretary of the VA armed forces cooperative study of the chemotherapy of tuberculosis and head of VA tuberculosis research in Washington. Dr. James W. Raleigh, of the VA hospital at Sunmount, N. Y., will become secretary of the VA armed forces study.

MISCELLANY

Brig. Gen. Thomas W. Mattingly, chief of the department of medicine at Walter Reed Hospital, will retire Aug. 31 after almost a quarter century of service. A heart specialist, he has been consulted in President Eisenhower's illness. He has pioneered in the use of teaching aids for group instruction in cardiology and conducted extensive clinical research, especially in coronary disease.

One recent seizure by the Food and Drug Administration involved "uranium" gloves and pads advertised as beneficial in treatment of arthritis and rheumatism. The manufacturer claimed the products had uranium dirt better than that used in "uranitoriums," but the FDA could detect no radioactivity in the articles. Criminal prosecutions included the successful action against a physician who sold an FDA inspector 55,000 amphetamine tablets for sale to truck drivers. The physician was sentenced to a three-year term.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice President.

1958 Clinical Meeting, Minneapolis, Dec. 2-5.

1959 Annual Meeting, Atlantic City, June 8-12.

1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

August

American Congress of Physical Medicine and Rehabilitation, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., Secretary.

American Hospital Association, Palmer House, Chicago, Aug. 18-21. Dr. Edwin L. Crosby, 18 E. Division St., Chicago 10, Director.

American Veterinary Medical Association, Sheraton Hotel, Philadelphia, Aug 18-21. Dr. J. G. Hardenbergh, 600 S. Michigan Blvd., Chicago 5, Executive Secretary.

Biological Photographic Association, Shoreham Hotel, Washington, D. C., Aug. 19-22. Miss Jane Waters, Box 1668, Grand Central P. O., New York 17, Secretary.

Chemical Organization of Cells, Normal and Abnormal, Madison, Wis., Aug. 21-23. Dr. J. F. A. McManus, Univ. of Alabama Medical Center, Birmingham, Ala., Chairman.

International College of Surgeons, Regional Meeting, Western Section, The Riverside Hotel, Reno, Nev., Aug. 21-23. For information address. Dr. Leo D. Nannini, 190 Mill St., Reno, Nev.

National Medical Association, Hotel Schroeder, Milwaukee, Aug. 11-14. Dr. John T. Givens, 1108 Church St., Norfolk, Va., Secretary.

Northwest Proctologic Society, Sun Valley, Ida., Aug. 27-29. Dr. John McKay, 645 Medical Dental Bldg, Seattle, Secretary.

Public Relations Institute, Drake Hotel, Chicago, Aug. 27-28. Mr. Leo Brown, 535 N. Dearborn St., Chicago 10, Director.

Rocky Mountain Radiological Society, Shirley-Savoy Hotel, Denver, Aug. 15-17. Dr. John H. Freed, Denver 20, Secretary.

West Virginia State Medical Association, The Greenbrier, White Sulphur Springs, Aug. 21-23. Mr. Charles Lively, P. O. Box 1031, Charleston 21, Executive Secretary.

World Medical Association, Copenhagen, Denmark, Aug. 15-20. Dr. Louis H. Bauer, 10 Columbus Circle, New York 19, Secretary-General.

September

American Academy for Cerebral Palsy, Sheraton-Biltmore Hotel, Providence, R. I., Sept. 25-27. Dr. Raymond R. Rembolt, University Hospitals, Iowa City, Ia., Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. Stewart Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

American College of Physicians, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., Council Chairman.

American Fracture Association, Skirvin Hotel, Oklahoma City, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

American Medical Writers' Association, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St, Quincy, Ill., Secretary.

American Roentgen Ray Society, Shoreham Hotel, Washington, D. C., Sept. 27-Oct. 3. Dr. C. Allen Good, 200, 1st St., S. W., Rochester, Minn., Secretary.

Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.

Kansas City Southwest Clinical Society, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 Gillham Rd., Kansas City 8, Mo, Executive Secretary.

Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Executive Secretary.

Michigan State Medical Society, Sheraton-Cadillac Hotel, Detroit, Sept. 30-Oct. 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich, Secretary.

Mississippi Valley Medical Society, Morrison Hotel, Chicago, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Montana Medical Association, Northern Hotel, Billings, Sept. 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings, Executive Secretary.

Nevada State Medical Association, Elko, Sept. 17-20. Mr. Nelson B. Neff, P. O. Box 188, Reno, Executive Secretary.

New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

Northeastern Section, American Urological Association, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

Oregon State Medical Society, Columbia Athletic Club, Portland, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

Tennessee Valley Medical Assembly, Read House, Chattanooga, Tenn., Sept. 29-30. Dr. Harry A. Stone, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Secretary.

Texas Academy of General Practice, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

Tri-State Medical Society, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clinic, Kings Highway, Shreveport, La., Secretary.

Utah State Medical Association, Hotel Utah, Salt Lake City, Sept. 9-12. Mr. Harold Bowman, 42 S. Fifth East St., Salt Lake City 2, Executive Secretary.

Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 20-22. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

Washington State Medical Association, Davenport Hotel, Spokane, Sept. 14-17. Mr. Ralph W. Neill, 1309 7th Ave., Seattle, Executive Secretary.

October

Academy of Psychosomatic Medicine, Park Sheraton Hotel, New York, Oct. 9-11. For information write Dr. Bertram B. Moss, Suite 1035 E. Washington St., Chicago 2.

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Academy of Pediatrics, Palmer House, Chicago, Oct 20-23. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill, Executive Secretary.

American Association of Medical Clinics, Palace Hotel, San Francisco, Oct. 2-4. Dr. John R. Hand, 1216 Southwest Yamhill St., Portland, Ore., Secretary.

American Association of Medical Record Librarians, Statler Hotel, Boston, Oct. 13-16. Miss Doris Gleason, 510 N. Dearborn St, Chicago 10, Executive Director.

American Association of Public Health Physicians, St Louis, Oct. 27-31. Dr. Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fla., Secretary.

American Association for the Surgery of Trauma, Drake Hotel Chicago, Oct. 2-4. Dr. William T. Fitts, Jr., 3400 Spruce St, Philadelphia 4, Secretary.

American Clinical and Climatological Association, Otesaga Hotel, Cooperstown, N. Y., Oct. 9-11. Dr. Marshall N Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

American College of Gastroenterology, Jung Hotel, New Orleans, Oct. 19-25. Mr. Daniel Weiss, 33 W. 60th St, New York 23, Executive Secretary.

American College of Surgeons, Conrad Hilton, Chicago, Oct 6-10 Dr. Michael L. Mason, 40 E Erie St., Chicago, Secretary.

American Dietetic Association, Bellevue-Stratford Hotel, Philadelphia, Oct. 21-24. Miss Ruth M. Yakel, 620 N. Michigan Ave, Chicago 11, Executive Secretary.

American Heart Association, Fairmont Hotel, San Francisco, Oct 24-25 Mr. John D. Brundage, 44 E. 23d St, New York 10, Secretary

American Otorhinologic Society for Plastic Surgery, Conrad Hilton Hotel, Chicago, Oct. 12. Dr. Josepr G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y, Secretary.

American Public Health Association, Kiel Auditorium, St Louis, Oct 27-31. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, Secretary

American School Health Association, St. Louis, Oct. 26-31. Dr. A. O. DeWeese, 515 E. Main St., Kent, Ohio, Secretary.

American Society of Anestesiologists, Penn-Sheraton Hotel, Pittsburgh, Oct. 19-24. Dr J. Earl Remlinger, 802 Ashland Ave, Wilmette, Ill., Secretary.

American Society of Plastic and Reconstructive Surgery, Drake Hotel, Chicago, Oct. 12-17. Dr. Kenneth L. Pickrell, Duke Univ Hosp., Durham, N. C, Secretary.

American Society for the Study of Arteriosclerosis, Hotel Whitcomb, San Francisco, Oct. 24-26. Dr. O J. Pollak, P. O. Box 228, Dover, Del, Secretary.

Association of American Medical Colleges, Ocean House, Swampscott, Mass., Oct. 13-15. Dr Richard H. Young, 303 E Chicago Ave., Chicago, Secretary

Association of Life Insurance Medical Directors of America, Statler Hotel, Hartford, Conn., Oct. 22-24. Dr. Royal S. Schaaf, P. O. Box 59 Newark 1, N. J., Secretary.

Association of Medical Illustrators, Dallas, Tex, Oct., Miss Rose V. Reynolds, 42d & Dewey Ave., Omaha 5, Secretary

Association of State & Territorial Health Officers, Hotel Washington, Washington, D. C., Oct. 22-24. Dr. Mack I. Stanholtz, State Office Bldg., Richmond, Va., Secretary.

Central Association of Obstetricians and Gynecologists, Hotel Leamington, Minneapolis, Oct. 2-4. Dr. Edwin J. DeCosta, 104 S Michigan Ave, Chicago 3, Secretary.

Central Neuropsychiatric Association, Deshler Hilton Hotel, Columbus, O, Oct 17-18. Dr. Ralph M. Patterson, Ohio State Univ, College of Med, Columbus 10, O., Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Oct. 31-Nov. 1. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Cleveland 6, Secretary.

Clinical Orthopaedic Society, Brown Palace Hotel, Denver, Oct 24. Dr. Charles H. Franz, 1801 Wealthy St. S. E., Grand Rapids, Mich., Secretary.

Congress of Neurological Surgeons, St. Francis Hotel, San Francisco, Oct. 29-Nov. 1. Dr. Richard L. DeSaussure, 899 Madison Ave, Memphis, Tenn., Secretary.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 23-24. Dr. J. J. Baehr, Jr., 117 N. Palafox St., Pensacola, Fla, Secretary.

Indiana State Medical Association, Murat Temple, Indianapolis, Oct. 13-15. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

Pennsylvania, Medical Society of the State of, Bellevue-Stratford Hotel, Philadelphia, Oct. 12-17. Mr. Lester H. Perry, 230 State St., Harrisburg, Executive Director.

Medical Society of Virginia, Hotel Jefferson, Richmond, Oct. 12-15. Mr. Robert I. Howard, 1105 W. Franklin St., Richmond 20, Executive Secretary.

National Proctologic Association, Hamilton Hotel, Chicago, Oct. Dr. George E. Mueller, 59 E. Madison St, Chicago 2, Secretary

Oklahoma City Clinical Society, Biltmore Hotel, Oklahoma City, Okla., Oct. 27-29. Mrs. Alma O'Donnell, 503 Medical Arts Bldg, Oklahoma City, Okla., Executive Secretary.

Southwestern Medical Association, Pioneer Hotel, Tucson, Ariz., Oct. 23-25. Dr. Russell L. Deter, 1501 Arizona St, El Paso, Tex., Secretary.

(Continued on page 30)

THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 15 CHICAGO, ILLINOIS AUGUST 9, 1958

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PENICILLINASE-PROVED ALLERGY TO PENICILLIN IN POLIOMYELITIS VACCINE

Murray C. Zimmerman, M.D., Whittier, Calif.

Six reactions in patients given injections of poliomyelitis vaccine were considered to be due to traces of penicillin present in the vaccine because each patient had had a previous similar reaction known to be due to penicillin allergy; the reaction after use of poliomyelitis vaccine duplicated the previous penicillin reaction; each patient obtained rapid clearing after being given a penicillinase injection (which would have no effect on anything but penicillin); and no recurrence followed subsequent administration of another brand of vaccine containing all the same allergens except penicillin. Patients with previous penicillin allergy should receive penicillin-free vaccines. If this is impossible, penicillinase should be given prophylactically preceding the vaccine injection. Before the use of penicillinase, a specific cause for reactions to poliomyelitis vaccine had been hard to prove. Such reactions could be due to chance, to psychic stress from the injection, to traces of a contaminant in the syringe, to intercurrent illness, or to a constituent of contaminant of the vaccine. The vaccine contains monkey protein, horse serum, formaldehyde, preservatives, and other antibiotics —all potential causes of reaction.

REACTIONS, usually urticarial, have developed after injections of poliomyelitis vaccine. These reactions might be due to chance, to psychic stress from the injection, to traces of a contaminant allergen in the syringe, to intercurrent illness, or to a constituent or contaminant of the vaccine. In six patients here reported, the reactions were considered due to traces (from 1 to 200 units per cubic centimeter) of penicillin present in poliomyelitis vaccine and were proved by (1) previous history of allergic reaction to penicillin, (2) present allergic reaction to poliomyelitis vaccine duplicating previous reaction known to be due to penicillin, (3) rapid clearing, after a single injection of penicillinase (a drug which destroys penicillin and has no effect on anything else), and (4) absence of further reaction when given a brand of poliomyelitis vaccine containing all the same components except penicillin (less than 0.001 units of penicillin per cubic centimeter).

Constituents of Poliomyelitis Vaccine

Contents[1] of poliomyelitis vaccine are as follows: 1. Medium 199, or modifications thereof. (This is an artificial cell culture medium. It contains vitamins and amino acids of small molecular size, probably not capable of sensitizing.) 2. Horse serum. (Final concentration in vaccine must be less than one part in one million. It is probably less than one part in five million.) 3. Phenolsulfonphthalein, 0.002%, as indicator dye. 4. Soluble monkey protein derived from blood or kidney. 5. Formaldehyde, 1:4,000 (may be neutralized to sodium bisulfite complex). 6. Preservatives (methylparaben and propylparaben, Wyeth; thimerosol [Merthiolate] plus tetrasodium salt of ethylene diaminetetraacetic acid [Versene], Lilly; benzethonium [Phemerol] chloride, Parke Davis; or other preservative, at

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manufacturer's discretion). 7. Poliomyelitis virus protein and nucleoprotein. 8. Antibiotics: penicillin, 200 units per cubic centimeter, and streptomycin, 200 units, are present in the original culture medium. Dilution, washing, filtration, and inactivation to produce the finished vaccine reduce this to between 1 and 30 units of penicillin per cubic centimeter. The manufacturer may reconstitute the culture by adding antibiotic to the original level, at two stages.

The original specification required 200 units of penicillin and 200 units of streptomycin per cubic centimeter of reconstituted tissue culture. This was modified on May 26, 1955, allowing manufacturers to stop reconstituting with these antibiotics. Wyeth Laboratories substituted polymyxin B for the reconstituted penicillin. The penicillin content of finished Wyeth vaccine[2] is below 0.001 units per cubic centimeter and probably below 0.000001 units. Finished vaccines of other manufacturers contain from less than one unit to a maximum of 200 units of penicillin per cubic centimeter. In response to letters, Parke Davis[3] stated, "as low as 3-10 units/cc."; Pitman-Moore,[4] "less than 20 U/cc."; and Lilly,[5] "15 U/cc., maximum." (Adenovirus vaccine is prepared in the same way as poliomyelitis vaccine, on the same monkey kidney tissue culture. It contains the same constituents, except that serotypes 3, 4, and 7 of adenovirus are substituted for poliomyelitis virus.)

Report of Cases

Six cases from private practice between May and November, 1957, indicate that penicillin reactions to poliomyelitis vaccine are relatively common. No search was made during the intensive mass immunization programs previously run, when tremendous numbers of patients were getting the vaccine. Many other cases of allergic reactions to poliomyelitis vaccine are known to me, but their cause was not proved.

Case 1.—This patient (of Dr. M. Knoll), with a previous history of penicillin allergy, was given a first injection of 1 cc. of poliomyelitis vaccine (Lilly). He developed a classic urticarial reaction 9 days later, and for 22 days was treated with ACTH, metasteroids, antihistamines, and sedation. His condition was improved, but never controlled, by heroic doses of steroids. On the 22nd day of his eruption, he received 800,000 units of penicillinase (Neutrapen). His symptoms disappeared in 24 hours, and all other medications were discontinued. There was no subsequent recurrence. Six months later, the patient was given 1 cc. of *penicillin-free* poliomyelitis vaccine (Wyeth), without reaction.

Case 2.—This 32-year-old man developed in three days a severe, acute, disabling, bullous dermatitis on the palms, soles, and medial thighs and oozing, infiltrated, nummular plaques on the arms and legs. He was diagnosed and treated for severe tinea pedis with "id." Since he stated that he had had a similar eruption twice before, each time after a penicillin injection, he was questioned in detail about possible recent penicillin exposures. He denied receiving medication of any sort. After three weeks of treatment with ACTH, wet dressings, and mild fungicides, he was seen by me while his regular doctor was on vacation. Since this patient had not improved, I requestioned him as to drug history. His statement, "You know, I had an eruption exactly like this twice before, each time after getting penicillin," made me ask again about penicillin, and he denied receiving it. Finally, I asked him specifically about poliomyelitis vaccine. The patient suddenly snapped his fingers and his head in a Hollywood "double-take." He said that he had had a "shot" of poliomyelitis vaccine during a free mass immunization drive and had completely forgotten about this.

He was immediately given his second injection of poliomyelitis vaccine (with penicillin) a few minutes after receiving 800,000 units of penicillinase. I believed that the penicillinase would destroy the remaining penicillin from his first injection of vaccine (29 days before) as well as that in his second. Since I did not want the effect of the penicillinase masked, all other therapy was stopped immediately. The patient's favorable response was complete and so dramatic as to provoke a report of "unbelievable" from his regular doctor, five days later. There was no recurrence. He was given Wyeth poliomyelitis vaccine, without reaction, four months later. (Previous vaccine was either Parke-Davis or Pitman-Moore.)

Case 3.—This 33-year-old woman (patient of Dr. P. Levan) had penicillin urticaria for three weeks, in January, 1957. She was well until October, 1957, when she received 1 cc. of poliomyelitis vaccine (either Parke-Davis or Pitman-Moore). Nine days later, she developed severe urticaria. Five days after the onset, she was given 800,000 units of penicillinase; the urticaria cleared in 72 hours, without recurrence. In December, 1957, 1 cc. of poliomyelitis vaccine (Wyeth) caused no reaction.

Case 4.—This patient (of Dr. J. Benson) had had chronic urticaria twice, each time after a penicillin injection. He had also developed mild, transient urticarial reactions after each ingestion of Roquefort cheese. The day after a 1-cc. injection of poliomyelitis vaccine (brand unknown), he developed a moderate urticarial response which continued for 16 days, in spite of administration of ACTH, antihistamines, and corticosteroids. On the 18th day after the poliomyelitis vaccine had been given, this patient received 800,000 units of penicillinase. All other therapy was discontinued. He was symptom-free in 24 hours, with no recurrence. Two weeks later, the patient was given 1 cc. of poliomyelitis vaccine (Wyeth), without reaction.

Case 5.—This 15-year-old girl denied any previous allergy to penicillin or allergy to two previous injections of poliomyelitis vaccine. She had her third injection of the vaccine Nov. 9, 1957. About Nov. 23, she gradually developed scattered blisters on palms and soles and peculiar round plaques on the arms and legs, up to 5 cm. diameter, of acuminate grouped fine papules. She received no treatment for this condition, which became progressively worse until Dec. 19. At this time, an allergic reaction to penicillin in poliomyelitis vaccine was considered possible but unlikely. The patient was given 800,000 units of penicillinase as a differential diagnostic measure. During the next 24 hours the blisters on her palms and soles disappeared almost completely and were gone in 72 hours. The plaques on the arms and legs showed rapid clearing and were completely gone in less than one week, without other therapy. Four weeks later 1 cc. of poliomyelitis vaccine (Wyeth) evoked no reaction.

Upon later questioning, the patient stated that she had had similar blisters on the palms and soles on two previous occasions, but much milder. These had cleared without treatment, and she was unable to recall whether they had followed the previous injections of poliomyelitis vaccine. She had had no penicillin in any other known form since 1955.

Case 6.—This 3½-year-old girl (patient of Dr. D. Freiburger) had a penicillin injection at age one year, followed by severe generalized exfoliative erythroderma, persisting through four weeks of hospitalization and steroid therapy. In April, 1957, she was given poliomyelitis vaccine (either Parke-Davis or Pitman-Moore), with no reaction. On Nov. 12, 1957, she was given her second injection of poliomyelitis vaccine, 1 cc. (Pitman-Moore). On Dec. 3, a severe generalized urticarial reaction started and became progressively worse on therapy with steroids, antihistamines, and starch baths. The patient finally required hospitalization. She was given 400,000 units of penicillinase on Dec. 13, with rapid, "dramatic" clearing in 24 hours. She was given a second 400,000 units on Dec. 16 (probably superfluous). All other therapy was discontinued. There was no recurrence of the reaction. She had no reaction after being given 1 cc. of Wyeth poliomyelitis vaccine on Dec. 23, 1957.

Comment

Since monkey protein,[6] horse serum, and formaldehyde, as well as antibiotics, may be allergens in very small dosage, it has been difficult to prove the cause of reactions subsequent to injections of poliomyelitis vaccine. Feinberg[7] reported the possibility of primary sensitization to penicillin in very low concentration and stated, "The amount of penicillin in polio vaccine is small, but judging by its activity as determined by us in tests of passively sensitized skin, it is sufficient to produce reactions in highly sensitive patients." Bierlein[8] reported a patient going into shock from an intracutaneous skin test with three one-millionths of one unit of penicillin. This patient had a passive transfer skin test positive to 1:25 dilution of poliomyelitis vaccine. Coleman and Siegel[9] showed in their patient that as little as one hundred-thousandth of one unit of penicillin could act as an eliciting dose for an allergic reaction. Clyde[10] reported a generalized urticarial reaction, starting one hour after a poliomyelitis vaccine injection, in a 12-month-old infant who had had a penicillin injection seven months earlier. This patient was given an injection of Wyeth poliomyelitis vaccine three months later, with no recurrence of symptoms. In spite of these reports, the literature is replete with assurances that the penicillin content of poliomyelitis vaccine is too small to be significant.

All previous therapy for allergic reactions has been nonspecific, suppressing symptoms rather than eliminating cause. This is no longer true for penicillin allergy. In vivo destruction of the penicillin antigen is now possible with penicillinase. Penicillinase is a protein enzyme, secreted by many strains of bacteria. It destroys penicillin, degrading it into a nonantigenic (and nonantibiotic) substance—penicilloic acid. Penicillinase has no effect on any other constituent of poliomyelitis vaccine. It has no effect whatever on any allergic reaction not due to penicillin.

By definition, the unit of penicillinase destroys in vitro one unit of penicillin in one minute, at 25 C and pH 7. The standard dose of penicillinase (Neutrapen), especially purified for parenteral injection in 2 cc. of sterile water, is 800,000 units. This is nontoxic and nonantigenic. It may produce local soreness and hence should be given deeply intragluteally. Penicillinase eliminated all symptoms of allergic reaction in about 95% of approximately 200 previously reported patients with penicillin allergy. Over 80% of patients obtain clearing of the reaction with one injection.[11] Penicillinase is the treatment of choice for penicillin reactions.

Summary

Penicillin is present in poliomyelitis vaccine (and adenovirus vaccine) in concentrations varying from 1 to 200 units per cubic centimeter, except in Wyeth poliomyelitis vaccine, which contains less than 0.001 units per cubic centimeter. There was sufficient penicillin in the vaccine (expect in one brand as reported in this paper) to cause allergic reactions in exceptional patients highly sensitive to penicillin. Six such allergic reactions, each duplicating a previous reaction known to be due to penicillin allergy, have been studied. The rapid clearing after one penicillinase injection and the lack of reaction to a brand of penicillin-free vaccine is offered as proof that penicillin, rather than some other allergen, was the cause of reaction in each patient. In patients with a history of penicillin allergy, penicillin-free vaccines should be used. If this is impossible, penicillinase should be given prophylactically preceding the vaccine injection.

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The penicillinase used in this study was supplied as Neutrapen, through Dr. B. Marr Lanman, SchenLabs Pharmaceuticals, Inc., New York.

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SCINTILLATING SCOTOMA

CLINICAL AND ANATOMIC SIGNIFICANCE OF PATTERN, SIZE, AND MOVEMENT

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Attacks of scintillating scotoma usually begin between the ages of 30 and 50 years and sometimes continue to recur indefinitely. The positive part of the scotoma, consisting typically of flickering colored and black zigzag lines, is followed by a negative part as it spreads out centrifugally over a definite portion of the patient's visual field. This process, which regularly takes about 25 minutes, is here analyzed with respect to the cerebral structures concerned. It is possible to calculate the rate at which the functional disturbance in the occipital lobe must be propagated in order to account for the rate at which the visual phenomena progress. There must be some uniform vascular change moving along the calcarine artery and successively affecting the parts supplied by its branches; in cases of migraine the change must move further on to affect adjacent parts. The significance of these attacks depends on the age of onset, and if they begin in persons of 60 years of age or older the usually harmless prognosis must be more guarded.

Scintillating scotoma presents a definite sequence of visual symptoms commonly associated as an aura with migraine. It could be considered a disease entity because it often occurs without headache or other sequelae.[1] The typical attack begins with a homonymous (bilateral equal size and position) blind spot just to the right or left of fixation which expands in diameter and in vertical length as it moves peripherally some 25 degrees over the duration of about 25 minutes (fig. 1). The leading edge of this negative scotoma is a positive and very conspicuous scintillating fortification figure. This term was suggested to early observers because of zigzag right angles as in a fort made to produce overlapping lines of fire.

Attacks of scintillating scotoma have been described more often in executive or professional groups studied.[2] During the first 10 minutes, the subject cannot read and would find driving in city traffic dangerous. One subject was perturbed because he could not read the telephone book to find his doctor's number. The attacks commonly come during activity, not relaxation. It has never been associated with epilepsy, but mental block or absentmindedness, numbness and tingling of an arm or leg, and partial amnesic aphasia have been described.

A doctor unfamiliar with the scintillating scotoma might think of apoplexy, cerebral aneurysm, or brain tumor. Regardless of the associated symptoms, the diagnosis of typical scintillating scotoma improves the prognosis so much that a neurologist is not generally consulted. In most cases where the patient is calm and observing, the symptom sequence can be described effectively and the diagnosis made by telephone. If the first symptoms occur in a patient aged 60 or more, the prognosis is not good [3] because of arteriosclerosis and impending vascular encephalopathy. The hemianopsia may be permanent in the senile patient.

Attacks of scintillating scotoma usually begin between the ages of 30 and 50 years and may continue indefinitely. It is considered familial and hereditary and may be due to a vessel anomaly in the visual cortex. The first account of scintillating scotoma without headache was apparently that of the English surgeon, John Abernethy, in 1826.[4] The relationship with migraine is usually considered one of degree of vascular spasm.[5] Migraine commonly stops at middle age, but scintillating scotoma does not.

The scotomas do vary from individual to individual and from attack to attack. They change sides or quadrants. One reputable observer [1b] stated that in his attacks, the horizontal median line appeared to be a barrier to the expansion of the scotoma. In my attacks, the scotoma may circle from five to one o'clock, counterclockwise. Two observers declared that the scotoma first appeared outside the 10 degree ring of the central field, but most observers portray it about 7 degrees from the fixation. It is agreed that the scotoma fades near the 30 degree ring or just outside the blind spot area. Figure 1 was drawn by me from sketches made during my second attack and agrees well with descriptions in the literature. The central field of one patient was taken by me on a tangent screen at the stage when the scotoma was about 10 degrees in horizontal diameter and well within the blind spot area. There was slight incongruity, but it probably corresponded to the time interval of testing first one eye and then the other.

I can confirm the observation [6] that the fortification figures are stronger and coarser in the lower fourth of the positive scotoma than above. The

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lines shown in figure 1 flash on and off in single right angle units at a rate of 8 to 12 times per second. Both the bright and the black phase are in strong contrast to the neutral gray seen inside the negative part of the scotoma. I found that the negative scotoma is best observed on printed matter, while the positive edge can be studied best against a dark background. These dazzling right angle units also move centrifugally like slightly oblique screw threads on a rotating gear and rotate also on their plane of extension perhaps 15 degrees, as suggested in figure 1. The lines are sun bright and sun color to me. A few reports in the literature mention spectral colors and Roman candle–like fireworks, but most observers have denied this.[7] It is interesting, and makes one wonder about the objectivity of the discussions, that nearly all the articles on the subject have been written by individuals subject to the attacks.

Inciting Causes

Inciting causes mentioned are fatigue, stress, emotional upset, and allergy to milk.[8] Attacks commonly follow high altitude flight or decompression to 20,000 ft., even in the absence of anoxia.[9] Cerebral angiograms are a common inciting agent.[10] Anoxia is commonly known to cause attacks.[11] Electrostimulation of the exposed visual cortex can excite scintillating scotoma.[11a] Only a small percentage of people develop the symptoms after such stimuli, and the scintillations are not always typical. A spontaneous attack of scintillating scotoma produced electroencephalographic changes similar to those of anoxia[12] and was attributed to constriction of the posterior cerebral artery.

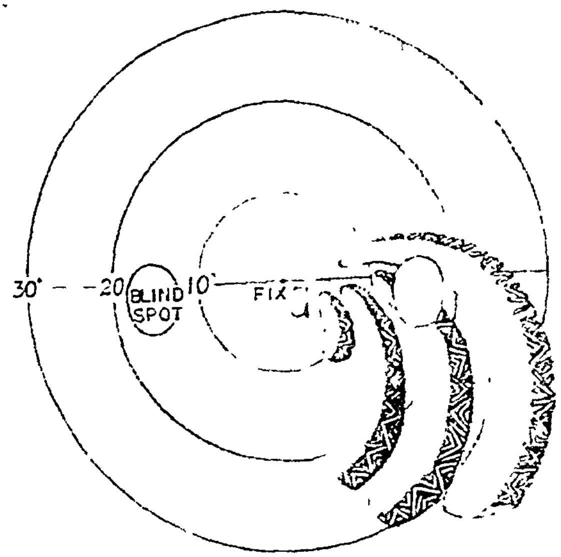

Fig. 1.—Scintillating scotoma expands gradually as it moves temporally at about one degree per minute. Negative portion appears neutral gray while positive leading edge is bright active show against black background.

In the case of a male patient of mine who was 30 years of age, frequent attacks of scintillating scotoma have apparently been cured by prescription of weak plus spheres worn constantly in glasses for the past two years. Jackson reported a similar case.[13]

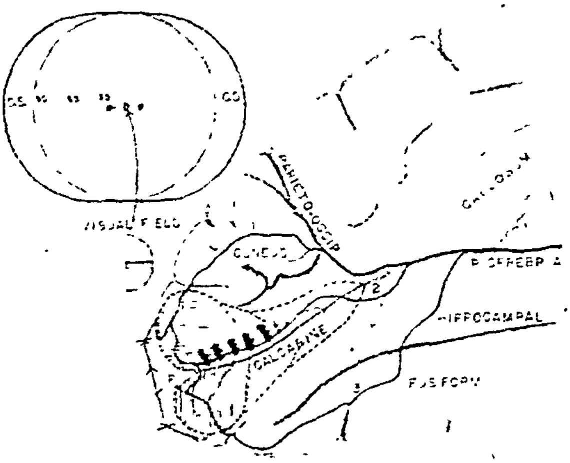

Fig. 2.—If scintillating scotoma appears in right visual field, it involves left visual cortex as indicated. Calcarine fissure divides cortex corresponding to the upper and lower field quadrants as indicated by vertical and horizontal lines. Expanding field defect corresponds to cortex irritation of constant size, moving from paramacular area along usual course of calcarine artery. Arteries numbered 1, 2, and 3, cuneus, calcarine, and temporo-occipital, are about 0.5 mm. in diameter in area outlined by dashed line of Gennari. Small branches not shown enter visual cortex in parallel rows. (Fissure is pressed open as indicated at "F".)

Theoretical Considerations

Abernethy,[4] in the belief that his scotoma was of retinal origin, relaxed and claimed to enjoy the entertainment of the dazzling procession across his visual field. Since it is homonymous, however, it can be agreed that the lesion is in the brain. The slight difference in binocular congruity reported by some observers would suggest a lesion in the optic radiation, but the positive nature of the scotoma indicates a location in the cortex or above. The fact that the scintillating fortification spectrums are two dimensional rules out higher centers such as area 18 or 19. Cerebral lesions above the visual cortex involve more color and form, with hallucinations.

The macular sparing, the progression across a line parallel to the calcarine artery (fig. 2), and the fact of induction by stress, high altitude, anoxia, allergy, and intra-arterial contrast mediums well establish the vascular origin of scintillating scotoma. If the disturbance originated in cortical cells or stroma, it should also involve the macular region and should spread in a less constant manner.

Figures 2 and 3 show that the area where the scotoma originates is supplied only by branches of the calcarine artery within the fissure. The artery itself at that level is only 0.5 mm. in diameter.[14] The macular area would not be involved in calcarine spasm because of anastomoses above and below and laterally. The denser, coarser appearance of the lower portion of the scintillating edge[6] would correspond to the upper limits of the cortical lesion most distant from the artery.

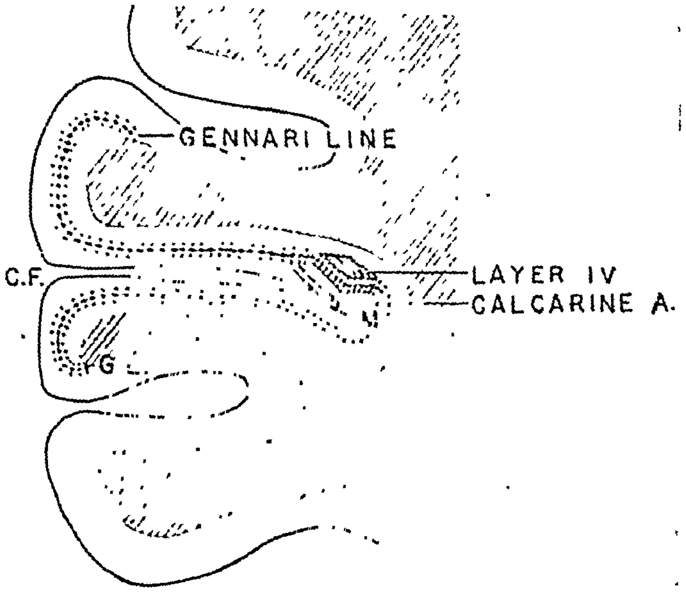

Fig. 3.—Cross section of visual cortex showing grossly position of visual sensory and fusion layer IV in usual relation to calcarine artery. "M" indicates macular representation.

Figure 4 shows a theoretical diagram of visual cortex cytoarchitecture suggested by the symptoms of scintillating scotoma. The rectilinear neuron pattern corresponds well to the "striate" layering found histologically[14] and to the patterns suggested by the facts of binocular fusion and space perception in the illustrations of Linksz.[15] There are individual variations in the position of the calcarine artery in the calcarine groove. An individual with two branches would probably not be among those having attacks of scintillating scotoma.

Figure 2 shows that the scotoma lesion moves within an area about 4 by 18 mm. and does not expand. The expanding sensory image is perfectly explained by the relative magnification of the retinal image representation on the cortex illustrated in figure 2. Notice that the small semicircle representing about 2 degrees of central field is magnified on the corresponding visual cortex 100 diameters,[6] the area with vertical and horizontal lines. The foveal cone affects about 100 cells in layers IVa to IVc. One cone in the fovea supplies a 0.25-mm. circle in the cortex,[14a] but one rod or cone in the periphery supplies an area as relatively small as the drop in visual acuity. The scintillating scotoma enlarges hundreds of times as it moves peripherally to 30 degrees, just as the cone density of the retina and relative visual acuity drops hundreds of times. Lashley[6] calculated from such considerations that the cortical lesion moved about 3 mm. per minute. More recent data would decrease this to less than 1 mm. per minute. Why the scotoma fades out at 30 degrees on the field remains unexplained. There must be some uniform vascular change with better anastomoses beyond this point or a decreased sensitivity to the irritation of peripheral cortical neurons. In migraine, the cortical irritation must move further on to other areas, but there has been no report of greater excursion of the scotoma. The scintillation has an off-on frequency of 8 to 12 per second. This frequency resembles that of two phenomena which might be related: (1) alpha rhythm, and (2) microfixation nystagmus.

Conclusions

Scintillating scotoma is a distinct entity commonly existing by itself, consisting of a paracentral homonymous scotoma which expands as it moves outward 30 degrees and which has a positive bright scintillating edge characterized by right angled lines. Attacks may occur in susceptible individuals daily, or as rarely as each six months, but the duration is regularly 25 minutes. Scintillating scotoma may occur as a preliminary aura to migraine, which can be considered in most cases a more extensive degree of the same vasomotor disease.

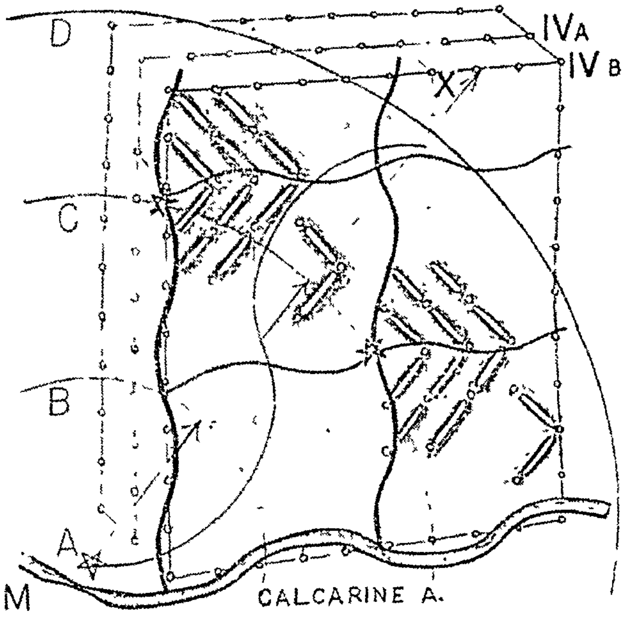

Fig. 4.—Section from figure 3 enlarged. Spasm theory is illustrated near the macula "M". Waves of stimulation and inhibition are suggested along line "AX" by sine wave. In destimulation area sensory cells involved form patterns determined by rectilinear anatomy of layer IV of cortex.

A third class of scintillating scotoma diseases should be distinguished when the symptom complex begins in persons of 60 years of age or more. This third class is complicated by superimposed arteriosclerosis, and the usually harmless prognosis must be more guarded. There may be permanent cortical changes with permanent hemianopsia and encephalomalacia in the more severe cases.

It remains to be determined why migraine commonly stops at age 45, while scintillating scotoma usually continues on. Perhaps accessory circulation can develop in the case of migraine and does not in the calcarine artery region.

The symptoms of scintillating scotoma confirm theories of the visual cortical cytoarchitecture, perhaps more exactly than have the anatomicopathological studies of the past and the studies based on visual space perception.

100 N. Euclid (8).

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CHRONIC SIALADENITIS

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Four cases have been selected to illustrate the insidious onset, slowly progressive course, and ultimate need of surgery in chronic sialadenitis. The four patients were all over 40 years of age and had long histories of peridontal disease. The submandibular glands and ducts were involved in every case, and sialoliths were found in three. The patients complained most of the difficulty in swallowing and the unsightliness of fibrotic swellings. Treatment consisted of excising the diseased structures and correcting the dental abnormalities. When the disease is recognized in its earlier stages, the underlying cause should be eliminated; otherwise recurrence and progression must be anticipated.

Chronic sialadenitis is an insidious, nonspecific, inflammatory disease of one or more salivary glands, manifested by intermittent swelling, and tending to progress, unless arrested, to formation of unsightly, fibrous tumors.

Ordinarily this disease occurs in middle or later life, affecting men more frequently than women. Occasionally it follows radiotherapy, ingestion of certain chemicals, acute salivary infection such as postoperative parotitis, and specific diseases such as mumps, tuberculosis, syphilis, and actinomycosis.[1] Occlusions of salivary ducts by tumors, foreign bodies other than calculi, and sources of extrinsic pressure such as scars are rare causes. Chronic sialadenitis may become seriously complicated by pyogenic bacterial invasion, usually associated with oral infection.

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New and Harper[2] reviewed 110 cases of nonspecific salivary gland inflammation. In 70 of these, calculi were found, 65 occurring in the submaxillary, three in the parotid, and two in the sublingual gland or duct. Forty cases without stone were also predominately submaxillary sialadenitis. Husted,[3] studying 63 patients with sialolithiasis, reported submaxillary stone in 60, with only three instances of parotid involvement. He noted that calculi consisted mainly of calcium salts, usually hydroxyl apatite, with which saliva was nearly always supersaturated. As pointed out by New and Harper and later by Schmidt-Neilsen,[4] since mandibular saliva was as a rule greatly supersaturated and parotid saliva generally much less so, preponderance of calculi in the submaxillary gland was partially explained on a purely chemical basis. The dependent location of Wharton's duct, especially favoring invasion of bacteria, also seemed to be an important factor.[5]

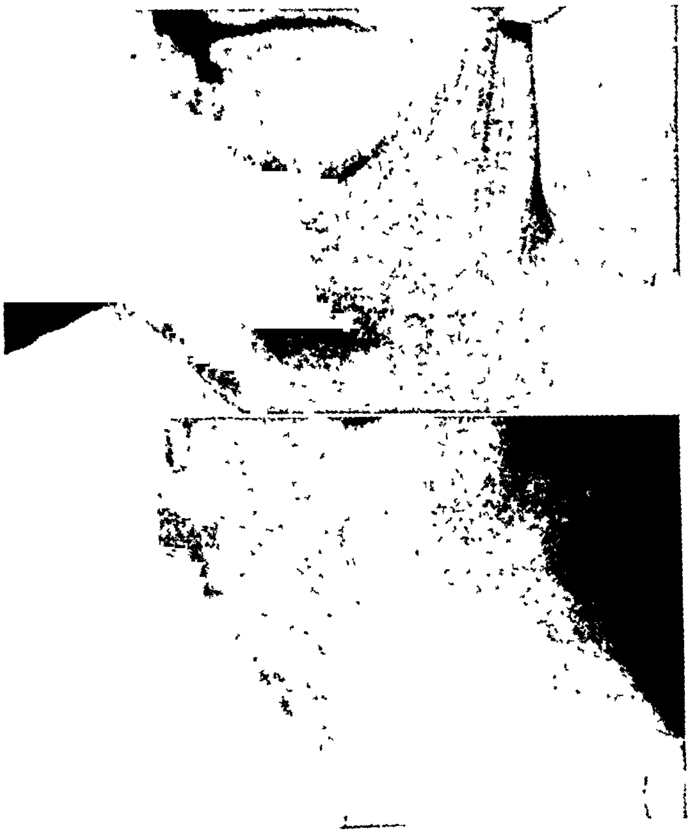

Fig. 1 (case 2).—Early chronic left submaxillary sialadenitis after salivary stimulation. The soft and diffuse swelling subsides almost entirely during quiescence.

Exemplary Cases

Four selected cases are presented to illustrate the typical onset, slowly progressive course, and final outcome of chronic sialadenitis.

Case 1.—Shortly after drinking a glass of tomato juice, a 50-year-old woman noticed diffuse bilateral swelling of the upper anterior part of the neck, which caused a frightening sense of tracheal constriction, lasted a short while, and then slowly subsided. Similar attacks followed, always after she had eaten sweet or sour foods, specifically, fruit juices, tomato juice, or anything seasoned with lemon or tomato. Swelling occasionally became alarming, but slowly subsided after cold applications and rinsing of the mouth with mild alkaline solutions.

Examination revealed extensive, bilateral, diffuse, soft, slightly tender submandibular swelling, extending downward as far as the laryngeal prominence, which subsided almost completely between attacks. Significant findings included severe pyorrhea, a devitalized tooth, and multiple periapical abscesses. Neither palpation of the salivary ducts nor roentgenologic examination demonstrated the presence of any salivary stones. Further examinations, including extensive and repeated sensitivity tests, were not contributory.

Upon advice of an oral surgeon all teeth were extracted and, after clearing up of infection, replaced with dentures. A bland diet was prescribed and use of a mild alkaline mouthwash during attacks advised.

Twenty years have passed without further progression. The patient avoids highly seasoned foods, but occasionally notices mild swelling from salivary stimulation, which she immediately controls by mouthwash. The submaxillary ducts are narrow, but patent. The glands are soft and not visibly enlarged. No stones have been found.

Case 2.—A 41-year-old man (fig. 1) noticed intermittent swelling beneath the left mandible, occurring while eating or shortly after, and associated with pain, fulness, constriction of the throat, and difficulty in swallowing. He had been edentulous for 15 years, but had recently received an injury of the jaw, followed by great discomfort on wearing of his dentures. There was tender, firm swelling of the left submandibular area, which later became less noticeable. Palpation of Wharton's duct was not contributory, but the shadow of a small stone was outlined in the submaxillary gland by roentgenography. The moderately enlarged gland, excised without difficulty, contained a stone which obstructed Wharton's duct at its origin. New dentures were prepared, removing a source of constant irritation.

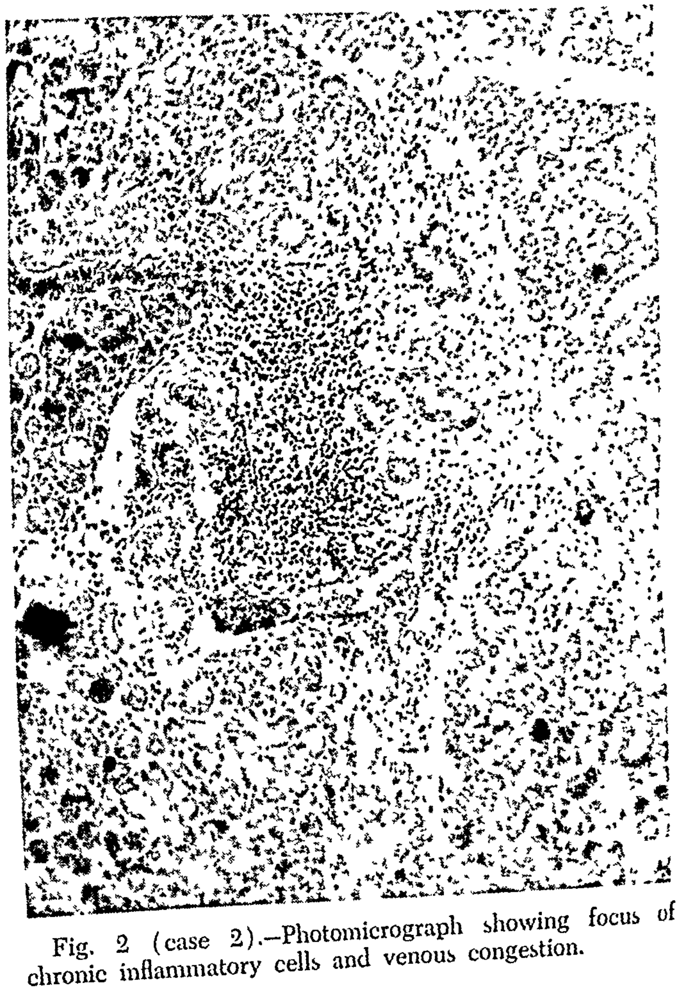

Fig. 2 (case 2).—Photomicrograph showing focus of chronic inflammatory cells and venous congestion.

Pathologist's Report.—The excised gland measured 3.5 by 3.5 by 3 cm. An irregular calculus, measuring 0.4 by 0.3 by 0.2 cm., was lodged in the inflamed, hyperplastic, and fibrotic salivary duct. Microscopic examination of sections revealed scattered foci of chronic inflammatory cells, consisting principally of lymphocytes, in or adjacent to the interlobular spaces. There was no appreciable loss of acinar tissue, but venous congestion and some generalized engorgement of the interlobular ducts with salivary secretion were observed (fig. 2).

Diagnosis.—The diagnosis was chronic submaxillary sialadenitis, mild, with obstruction of Wharton's duct by a sialolith.

CASE 3.—A 58-year-old man complained of bilateral firm tumors below the mandible, first noticed two years previously. These had slowly enlarged since onset, becoming more swollen for short periods after eating highly seasoned foods and causing considerable difficulty when he swallowed.

Examination revealed very hard, smooth, bilateral submaxillary tumors (fig. 3). Very poor carious teeth, periapical abscesses, and severe pyorrhea first necessitated extraction of all remaining teeth and replacement with dentures. The right submaxillary gland was then excised and was found to contain an irregular stone, 5 mm in diameter, obstructing the duct at its origin. Two weeks later the left submaxillary gland was excised and, although histologically identical with that of the opposite side, did not contain a stone.

Pathologist's Report.—The ovoid, right submaxillary gland measured 5 by 3.5 by 2.5 cm. Cut surfaces revealed multiple small cystic spaces containing thick mucoid fluid. The duct contained a sialolith. The left gland, measuring 4.0 by 3.3 by 1.5 cm., was firm and fibrous. Microscopic examination of sections from both glands revealed an identical histopathological picture (fig. 4) The cystic spaces consisted of multiple dilated salivary ducts, or sialoceles. Throughout both glands the periductal and interlobular connective tissue was strikingly thickened and hyalinized, widely separating the lobules. There was very little acinar tissue, the greater part having been replaced by interstitial fibrous tissue. The intralobular ducts were dilated, contained inspissated plugs of secretion, and were surrounded by collars of hyalinized or edematous laminated fibrocollagenous tissue. The lobules were infiltrated by lymphocytes, monocytes, and plasma cells. Frequently, lymph patches, often complete with germinal centers, were found. The larger arteries showed intimal fibrosis. Many smaller arteries and arterioles were partially hyalinized. Few capillaries, veins, and lymph vessels were observed.

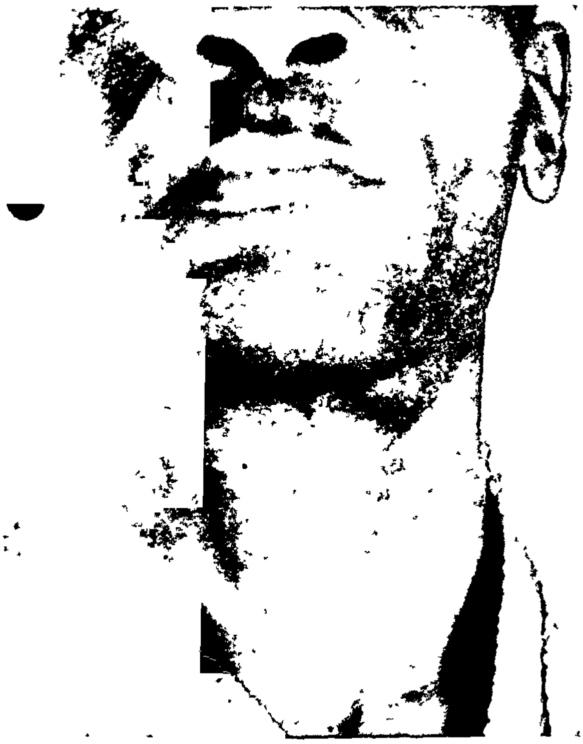

Fig. 3 (case 3).—Advanced bilateral chronic submaxillary sialadenitis, during quiescence. These hard tumors, indistinguishable from other neoplasms, must be excised.

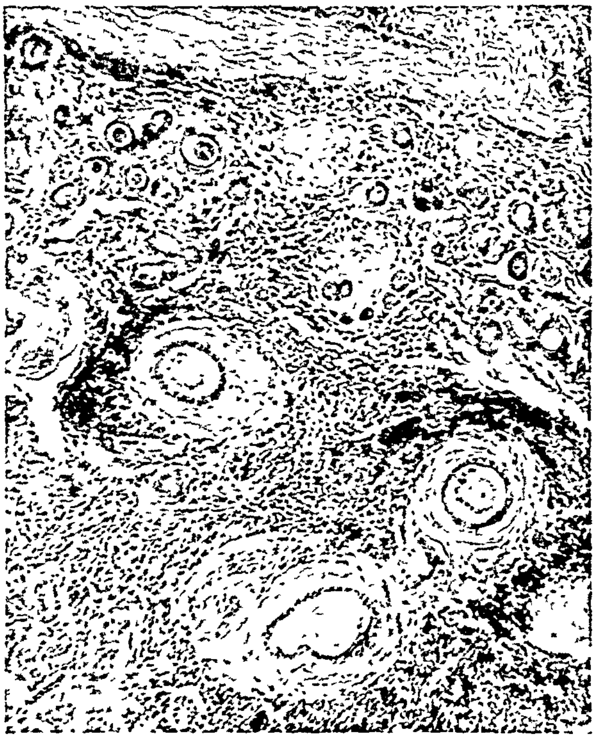

Fig. 4 (case 3).—Photomicrograph showing loss of acinar tissue, thickening of interlobular connective tissue; laminated collars of fibrocollagenous tissue surrounding many ducts filled with inspissated saliva, and infiltration with chronic inflammatory cells

Diagnosis.—The diagnosis was chronic submaxillary sialadenitis, bilateral, severe, and calculus in the right submaxillary duct.

CASE 4.—A 57-year-old man presented himself because of unsightly tumors, located bilaterally in the submandibular area. These had first appeared as small nodules four years previously and had grown slowly and steadily. Swelling had first been intermittent, associated with seasoned foods, but was now constant. He had no discomfort other than difficulty in swallowing. He reported considerable past difficulty with dental caries and had lost most of his teeth.

Examination revealed large, smooth, firm, bilateral masses which protruded below the mandible (fig. 5). Two broken teeth, roots from seven others previously destroyed, periapical abscesses, and severe pyorrhea were found. Palpation of the salivary ducts and roentgenologic examination failed to demonstrate calculi either in the ducts or in the glands, although shadows of very small calcific flecks appeared within the gland substance.

All tooth remnants were extracted and dentures fitted. The right submaxillary gland was removed with difficulty because of complete fibrosis and firm attachment by fibrous adhesions to adjacent structures. After excision of the gland a rigid, thick-walled cavity remained, which was slowly obliterated with pressure and considerably delayed healing. Similar difficulty was later experienced upon excision of the left gland.

Pathologist's Report.—The right submaxillary gland, weighing 35 Gm. and measuring 5 by 4 by 3.5 cm., had a uniformly hard and woody consistency. The organ was slightly lobulated and had an irregular contour. Cut surfaces were grey-white and gritty. The left gland was irregular, nodular, and measured 4.5 by 4.3 by 3.5 cm. It had an almost cartilage-like consistency. Microscopically, these glands were almost completely replaced by vascular hyalinized scar tissue (fig. 6). This extended beyond the confines of the glands into adjacent areolar tissue. The lobular structure of the glands was almost entirely lost. Occasional patches of lymphocytes and dilated atrophic salivary ducts occurred in the scar tissue. These surviving ducts were heavily plugged by masses of inspissated secretion. Frequently, calcific deposits occurred in these plugs. Sometimes the ductal epithelium about such plugs had disappeared and was replaced by foreign body giant cells. Chondral and osteoid metaplasia was seen in the dense scar tissue. Rare surviving lobules were heavily infiltrated by chronic inflammatory cells, chiefly lymphoid, and contained little if any acinar tissue. The picture was that of virtually complete fibrous replacement, with obstructive phenomena.

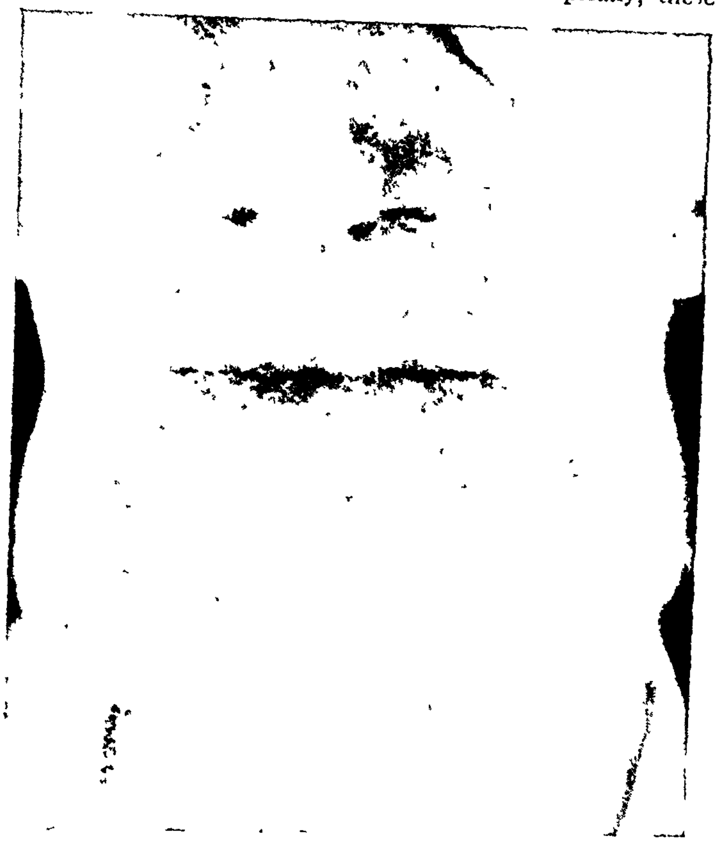

Fig. 5 (case 4).—Terminal bilateral chronic submaxillary sialadenitis. These fibrosed glands no longer respond to salivary stimulation, are extremely unsightly, and are difficult to excise.

Diagnosis.—The diagnosis was chronic submaxillary sialadenitis, terminal stage, with obstructive phenomena of long duration, and multiple small sialoliths within both glands.

Comment

The first case represented early sialadenitis, with arrest of the process after removal of all sources of infection. The narrow salivary ducts remained sufficiently patent to accommodate ordinary salivary flow. In case 2, the disease was somewhat more advanced but still comparatively mild and involving one submaxillary gland, and was complicated by a stone, obstructing the duct at its origin and necessitating removal. In case 3 the disease had progressed to advanced fibrosis, with considerable loss of acinar tissue and extensive chronic inflammation. The bilateral hard tumors required excision because of unsightly appearance, pressure symptoms, and need for diagnosis of the firm neck tumors. It is of interest that the right gland, obstructed by a stone, was histologically identical with the stoneless one of the left side. In the fourth case the disease had reached the final stage, typified by unsightly, painless, hard, fibrous tumors, unaffected by salivary stimulants, causing only pressure symptoms. Both submaxillary glands were virtually replaced by dense scar tissue, with chondral and osteoid metaplasia. Inflammation had spread to adjacent structures, attacking all tissue planes and rendering removal extremely difficult.

These examples clearly illustrate the progressive inflammatory reaction of salivary glands, caused by ductal occlusion, often associated with oral infection. Sialolithiasis, as part of the process, frequently develops in accumulated inspissating saliva, supersaturated with calcium salts. Remission of early sialadenitis may be expected after reestablishment of adequate and sustained drainage.[6]

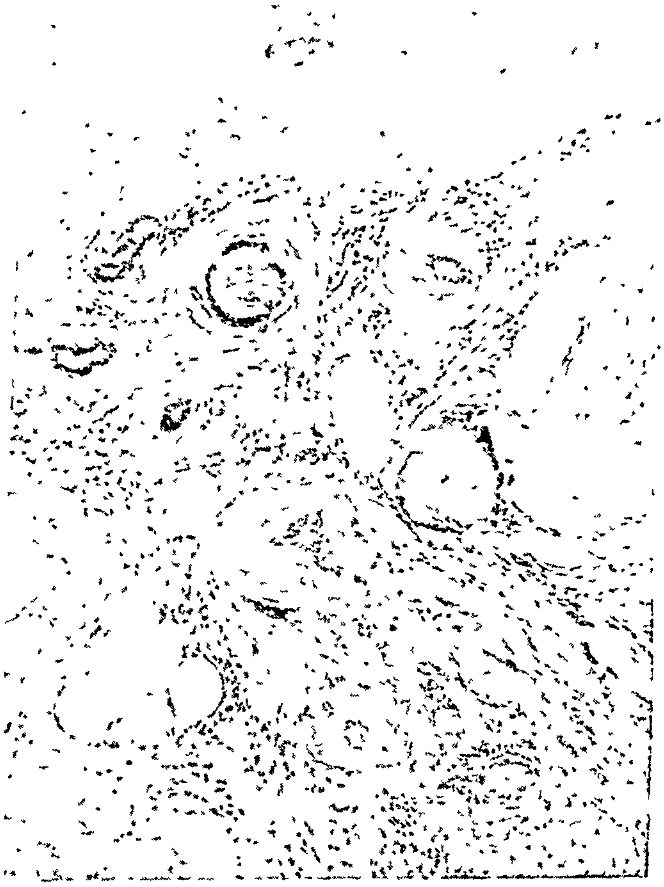

Fig. 6 (case 4).—Photomicrograph showing loss of lobular structure, almost complete replacement by hyalinized scar tissue, and few surviving ducts, heavily plugged with inspissated saliva. Foreign body giant cell reaction occurs near center of field in plug of secretion, devoid of surrounding ductal epithelium.

Wharton's duct, lying throughout its relatively great length between the base of the tongue and the lower jaw, is particularly susceptible to infection. This, plus high supersaturation of calcium salts in submaxillary saliva, provides an *ideal site* for both obstruction and stone formation, thus accounting for the overwhelming comparative incidence of submaxillary gland involvement.

Summary

Chronic sialadenitis is a progressive inflammatory process of one or more salivary glands, caused by ductal obstruction, with stasis and inspissation of saliva. Oral infection is often associated with ductal obstruction and further complication from pyogenic bacterial invasion. This disease, recognizable at onset, usually subsides upon accomplishment of early and sustained drainage, frequently by mere removal of a ductal stone. Unless the underlying cause, generally oral infection, is eliminated, recurrence and progression may be anticipated. The resulting fibrous tumors, indistinguishable from neoplasms, must be excised.

Box 30, Veterans Hospital (Dr. King).

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MACROGLOBULINEMIA–REPORT OF FOUR CASES

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and
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Macroglobulinemia is the presence of globulins of high molecular weights (near one million) in abnormally high concentrations in the blood serum. It is generally accompanied by mucosal bleeding, blurring of vision, lymphadenopathy, hepatosplenomegaly, and anemia. The dimness of vision is explained by severe engorgement of the retinal vessels observed during examination of the fundus oculi. The macroglobulinemia is demonstrated by methods of protein analysis involving the use of the ultracentrifuge. The clinical and laboratory findings in four cases are given in detail; the patients were two men aged 50 and 76 and two women aged 58 and 68 years. This combination of symptoms and laboratory findings should be thought of as a syndrome rather than a disease. The cause is undetermined, no reliable treatment is known, and the outcome in a given case cannot be predicted.

A number of diverse clinical conditions have in common qualitative or quantitative abnormalities of plasma proteins. Among the more interesting of the pathological proteins are the globulins of high molecular weight, or the macroglobulins, the presence of which can be confirmed only by the ultracentrifugation technique of protein analysis. Trace amounts of macroglobulins can be found in normal serums, so the term "macroglobulinemia" arbitrarily is reserved for serums containing more than 5% of components sedimenting at ultracentrifugation with Svedberg constants greater than 15, or more than S15. Waldenström,[1] in 1948, first outlined the clinical features in six patients who had a fraction in the serum proteins with molecular weights near one million. A number of authors subsequently have reported clinically similar cases under the term "macroglobulinemia of Waldenström."

This report presents a brief discussion of macroglobulinemia, along with an analysis of the clinical features in four cases encountered at the Mayo

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Clinic. The appearance of the ocular fundus in this syndrome will be described. The morphologic abnormalities in the bone marrow, the natural course of the syndrome, and problems in therapy will be emphasized.

Report of Cases

Case 1.—A 50-year-old man came to the Mayo Clinic in March, 1956, because of visual blurring that interfered with his work and that had been present for four months. He had suffered from rheumatoid arthritis for 12 years. Enlargement of the spleen had been noted three months prior to our examination, and epistaxis had occurred frequently during the same period.

Results of a general examination were normal except for some residual joint deformities of rheumatoid arthritis, shotty enlargement of lymph nodes, and hepatosplenomegaly. Examination of the ocular fundi revealed tremendous engorgement of the retinal veins. In the left eye, the nerve head was elevated 1 D. by edema and the veins were engorged, but the arteries were normal. A number of zones of hemorrhage were scattered throughout the lower portion of the retina of this eye.

Pertinent laboratory data were as follows: The hemoglobin level was 11.4 Gm. per 100 ml. of blood; erythrocytes numbered 4,700,000 per cubic millimeter of blood, and the leukocyte count was 2,400. The differential leukocyte count revealed 46% lymphocytes, 15% monocytes, 36% neutrophils, 1.5% basophils, and 1.5% eosinophils. The erythrocytic sedimentation rate was 96 mm. during the first hour (Westergren method). The blood platelet level was 177,000 per cubic millimeter, and the reticulocyte count was 0.7%. The bleeding time was four minutes. Total serum proteins measured 10.6 Gm. per 100 ml., with 2.5 Gm. of albumin and 8.1 Gm. of globulin. A serologic test for syphilis was nonreactive. Urinalysis yielded normal results. Serum electrophoresis revealed the albumin fraction to be 2.81 Gm., alpha-1 globulin 0.36 Gm., alpha-2 globulin 0.73 Gm., beta globulin 0.94 Gm., and gamma globulin 5.26 Gm. The bone marrow contained increased numbers of lymphocytes and mature plasma cells.

Ultracentrifugation revealed that approximately 42% of the serum proteins consisted of macroglobulins, distributed as follows: S14 components, 5.8%; S20 components, 23.7%; S23 components, 3.6%; others, 9.1%.

This case was of interest because disabling blurring of vision was the complaint that brought the patient to a physician. This disturbance appeared to be directly related to venous stasis produced by the large viscous protein molecules.

Case 2.—A 68-year-old woman came to the clinic in April, 1956, because she had noted swollen "glands" under both arms for three months. During the previous year, she had experienced increasing weakness, moderate dyspnea with exertion, and a nonproductive cough. Her home physician had discovered anemia and had given her injections of liver extract and five blood transfusions. Rather profuse bleeding had followed dental extractions four weeks previously, and some spontaneous bleeding from the gums had occurred recently. Blurring of vision was a major concern to the patient, as she could not read any but the largest print without resorting to the use of a magnifying glass.

Examination revealed prominent enlargement of the anterior cervical, supraclavicular, axillary, epitrochlear, inguinal, and popliteal lymph nodes. The spleen was palpable 2 to 3 cm. below the left costal margin, but the liver could not be palpated. Funduscopic examination disclosed huge retinal veins estimated to be four or five times normal size, along with many scattered zones of retinal hemorrhage and exudates. The ophthalmologist considered the retinopathy to be that of a blood dyscrasia and wondered if the patient might have multiple myeloma.

The urinalysis was normal. The value for hemoglobin was 8.0 Gm.; the erythrocyte count was 2,590,000 per cubic millimeter and the leukocyte count was 12,800. Differential blood cell counts revealed 42.5% lymphocytes, 4.5% monocytes, 41% neutrophils, 1.5% eosinophils, 1% basophils, and 9.5% prolymphocytes. Platelets numbered 129,000 per cubic millimeter; the coagulation time was 12 minutes, and the bleeding time was 3 minutes. The erythrocytic sedimentation rate, done routinely, was 1 mm. The blood urea level was 36 mg. per 100 ml. Serum electrophoresis revealed the albumin fraction to be 3.34 Gm., alpha-1 globulin 0.36 Gm., alpha-2 globulin 0.62 Gm., beta globulin 0.56 Gm., and gamma globulin 5.51 Gm. The bone marrow had reduced cellularity. A pronounced increase in mature plasma cells was apparent in some regions, whereas lymphocytes predominated in others. Erythropoiesis was reduced. Biopsy of an axillary lymph node revealed infiltration by mature lymphocytes as well as by plasma cells; many of the latter had lymphoid characteristics. Ultracentrifugation demonstrated that 40% of the serum protein consisted of macroglobulins.

It is of interest that difficulty with vision also was a serious problem in this patient. Its relationship to her primary disease had not been recognized earlier by either the patient or her physician. It is of interest further to note the sedimentation rate of 1 mm. in the face of such a great increase in gamma globulin. This is probably a reflection of the tendency of these serum proteins to gel on cooling.

Case 3.—A 76-year-old man was examined in December, 1955, because of swelling of his legs of two months' duration. The patient had come to the clinic on four previous occasions since 1943. His initial examination (1943) had been prompted by hoarseness, and idiopathic paralysis of the left vocal cord was discovered. At that time, urinalysis had revealed grade 3 albuminuria and Bence Jones proteinuria. The sedimentation rate was 35 mm., and a differential blood cell count revealed 17% monocytes. Plasma cell (multiple) myeloma was suspected, but study of sternal bone marrow did not confirm this diagnosis. Marrow smears revealed an increase in both lymphocytes and plasma cells, but typical "myeloma cells" were not seen. When he had been re-examined on other occasions (1949, 1952, and 1953), Bence Jones proteinuria and albuminuria were persistently present. The marrow pattern had remained unchanged. The patient had not complained of any visual disturbances, but the ophthalmologist had noted engorgement of the retinal veins of both eyes in 1952. Some diffuse osteoporosis was apparent in roentgenograms of the skull and spinal column, but focal osseous lesions were absent. The blood urea level ranged from 32 to 46 mg. During this entire period, the serum globulins had been greatly increased, ranging from 6.0 to 7.4 Gm. Cryoglobulins were absent.

In 1952, the patient had experienced massive gastrointestinal hemorrhage, for which 10 blood transfusions of 500 ml. each were given. A second episode of hematemesis and melena had occurred two months prior to his most recent examination. The patient denied having had epistaxis or purpura.

Examination in December, 1955, revealed severe pitting edema of the lower extremities, a right inguinal hernia, and benign prostatic enlargement. The spleen and liver were not enlarged, and significant lymphadenopathy could not be detected. The funduscopic appearance was normal except for engorgement of the retinal veins.

Urinalysis revealed grade 3 albuminuria and Bence Jones proteinuria. The hemoglobin level measured 9.2 Gm.; the erythrocyte count was 2,650,000 per cubic millimeter, and leukocytes numbered 5,300. The differential blood cell count revealed 35.5% lymphocytes, 15% monocytes, 47.5% neutrophils, and 2% eosinophils. The platelet count was 173,000 per cubic millimeter. The sedimentation rate was 137 mm. Total serum proteins measured 8.87 Gm., with 2.82 Gm. of albumin and 6.05 Gm. of globulin. The value for serum calcium was 11.7 mg. per 100 ml. and that for phosphorus was 3.4 mg. The blood urea level was 42 mg. A roentgenogram of the thorax revealed torsion of the aorta and a Ghon complex, while roentgenograms of the stomach and duodenum showed no abnormalities. Roentgenograms of the skull and spinal column revealed diffuse osteoporosis.

Serum electrophoresis gave a value for albumin of 2.22 Gm., alpha-1 globulin 0.24 Gm., alpha-2 globulin 0.54 Gm., beta globulin 0.76 Gm., and gamma globulin 3.89 Gm. The bone marrow showed increased numbers of lymphocytes and plasma cells; the latter were for the most part mature, although occasional immature forms were present. Increased numbers of tissue mast cells were present. Ultracentrifugation revealed that 47% of the serum proteins consisted of macroglobulins (S18, 38.7%; S25, 6.5%; and S32, 1.5%).

This case is unique in that, despite the observed long course and the continuous presence of Bence Jones proteinuria for 14 years, the blood urea level was always normal. It is also interesting that neither lymphadenopathy nor splenomegaly developed during this long period of observation. Mucosal bleeding, so frequently seen in this syndrome, did not occur, although massive gastrointestinal bleeding was present. It is of further interest that, while the patient had massive amounts of macroglobulins in his serum, microglobulins (Bence Jones proteins) with the same electrophoretic mobility were continuously being excreted in the urine throughout this long period.

Case 4.—A 58-year-old woman was re-examined at the clinic in March, 1956. She complained of weakness, easy fatigability, and shortness of breath of six years' duration. During the same period, the patient experienced almost daily epistaxis. Her original examination at the clinic was conducted in 1951, at which time almost identical complaints had been present. Examination at that time had revealed a few shotty cervical and supraclavicular lymph nodes, pallor, and minimal splenomegaly. Urinalysis disclosed grade 2 albuminuria but no Bence Jones protein. The erythrocyte count was 2,160,000 per cubic millimeter and leukocytes numbered 9,000. The value for hemoglobin was 7.0 Gm. per 100 ml. A differential count revealed 50% lymphocytes, 9% monocytes, 37.5% neutrophils, 1% metamyelocytes, and 2.5% myelocytes. The sedimentation rate was 141 mm. The platelet count was 165,000 per cubic millimeter. Serum proteins totaled 10.33 Gm., with 2.44 Gm. of albumin and 7.89 Gm. of globulin. A test of liver function using sulfobromophthalein gave normal results. Cryoglobulins were not found. Roentgenograms of the thorax, stomach, spinal column, and skull showed nothing abnormal. Biopsy of a lymph node disclosed only inflammatory changes, with an increase in plasma cells. The bone marrow contained increased numbers of lymphocytes and plasma cells, with lymphocytes predominating. Definitive diagnosis was not established, but malignant lymphoma or plasma cell myeloma was regarded as most likely. A total of 27.2 mg. of nitrogen mustard was administered. The patient felt improved subjectively and gained 10 lb. (4.5 kg.), but little objective improvement could be detected. A second course of nitrogen mustard given five weeks later was followed by further subjective improvement, but again there was no significant change in the patient's physical or laboratory status, other than perhaps some lessening of her transfusion requirements.

From 1951 to 1956, the patient's course remained much the same. Although she continued to tire easily and have frequent mild epistaxis, she was always well enough to carry on most of her household activities. Periodically, her home physician administered blood for the persistent anemia. Whole body irradiation was given in October, 1955, with no observable benefit. A brief trial of prednisone therapy was of no help. The patient was re-examined at the clinic on a number of occasions. Repeated aspiration of sternal marrow always revealed essentially the same morphologic changes. More prominent lymphadenopathy gradually developed and the spleen also increased in size. Another biopsy of a lymph node in October, 1955, disclosed nothing of diagnostic value. Continued postoperative oozing of blood from the biopsy site required administration of 500 ml. of whole blood and re-exploration of the wound.

The patient's vision was excellent, but ophthalmoscopic examination revealed huge and uniformly dilated retinal veins. The peculiar funduscopic picture was considered to resemble that of angiomatosis retinae of Lindau except that direct arteriovenous connections were absent. Serum electrophoresis revealed a value for albumin of 2.33 Gm., alpha-1 globulin 0.36 Gm., alpha-2 globulin 0.59 Gm., beta globulin 0.59 Gm., and gamma globulin 8.23 Gm.

Ultracentrifugation in October, 1955, demonstrated 65% of the serum proteins to be macroglobulins (S20, 50%; S25, 12%; and near S30, 3%).

This patient's course also was chronic. Throughout the entire six-year period of observation, she was able to carry on most of her household activities despite pronounced hypergammaglobulinemia, anemia, and almost daily epistaxis. No response followed the use of prednisone or whole body irradiation, although some subjective improvement followed administration of nitrogen mustard. This case also serves to point out that protracted oozing of blood might follow even minor surgical procedures, obviously adding to their risk.

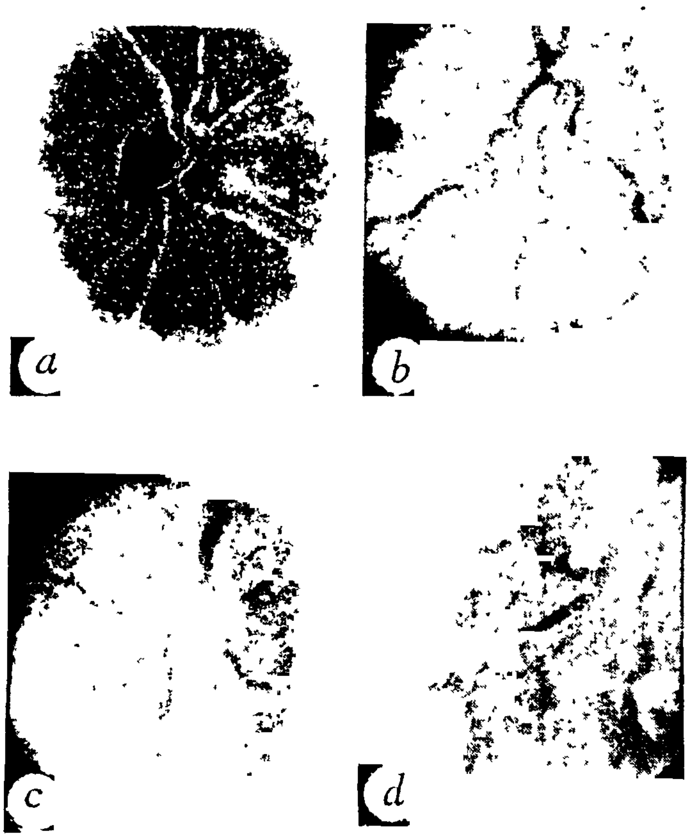
Comment

The clinical picture is not uniform in all patients who have large quantities of macroglobulins, but a number of features occur often enough to be considered characteristic. The syndrome occurs predominantly in persons beyond the age of 50 years and has been reported more frequently in men. While cutaneous purpura is rare, mucosal bleeding, particularly from the nose and gums, occurs frequently. Enlargement of lymph nodes and hepatosplenomegaly often occur but are not invariable. Blurring of vision is sometimes disabling and may be the presenting symptom. Focal osseous lesions of the type seen in plasma cell myeloma have not been reported.

A number of abnormalities in laboratory data are noted regularly. The peripheral blood usually gives evidence of mild or moderate normochromic and normocytic anemia. Lymphocytosis or monocytosis may be present. Great increase in the sedimentation rate occurs in almost every case. Exceptionally high serum viscosity is found, and spontaneous gelling of the serum on cooling may occur. Hyperglobulinemia is present, and serum electrophoresis reveals a peak in the beta or gamma globulins. Ultracentrifugation discloses that the globulin is of high molecular weight, with sedimentation coefficients of 17 to 20 Svedberg constants.

The appearance of bone marrow in macroglobulinemia is decidedly abnormal, although the changes are not diagnostic. In most cases, the cellularity of the marrow is reduced. Infiltration by both lymphocytes and plasma cells is noted, and in many instances the two lines of cells appear to merge, with curious transitions from lymphoid cells to plasma cells. The plasma cells are for the most part mature, and the cytoplasm of the lymphocytes is often scant. Tissue mast cells may be present.

The ocular fundus in macroglobulinemia is distinctive (*see figure*). The retinopathy is similar to that seen in plasma cell myeloma, although the dilatation of the veins is usually more pronounced in macroglobulinemia. The retinal veins may be tremendously engorged in some instances, being four or five times normal size. Scattered zones of hemorrhage and exudates may be seen. The ophthalmoscopic picture has been reported in the foreign literature [2] but, to our knowledge, it has not been described in the United States. In two of our four cases, visual complaints were the primary factor bringing the patients for examination; in one of these two cases, the ophthalmologist first suggested the possibility that a disturbance in blood proteins might be present.



Fundus photographs: *a*, normal appearance; *b*, *c*, and *d*, appearance in cases 1, 2, and 4 respectively.

Properly considered, macroglobulinemia should be looked on as a syndrome rather than a specific disease entity. The cause is obscure, although it appears to be associated with or to result from a disturbance of the reticuloendothelial system, with resultant lymphoid-plasmacytoid proliferation. Macroglobulins presumably are produced by the abnormal plasma cells and lymphocytes, although definite proof of this is lacking. Most immunological studies with macroglobulins, as with proteins in myeloma, indicate that these proteins have an immunological specificity differing from that of normal proteins.[3]

A precipitin test using rabbit antimacroglobulin serum that had been absorbed with normal serum gave positive reactions in 14 of 16 cases reported by Habich and Hässig.[4] It also has been noted that macroglobulins from several patients were individually specific and immunologically different from other macroglobulins.

The so-called Sia test, involving addition of several drops of serum to a test tube of distilled water, has been suggested as a possible screening test for the presence of macroglobulins,[5] but experience has shown that both falsely positive and falsely negative results occur.[6] Therefore, ultracentrifugation is necessary for demonstration of the presence of macroglobulins.

The syndrome of macroglobulinemia must be differentiated from plasma cell myeloma, chronic lymphocytic leukemia, malignant lymphomas, and so-called idiopathic hypergammaglobulinemia. The prognosis is variable but this diagnosis is compatible with survival for many years, as exemplified in two of our four cases.

Treatment is usually ineffective. Cortisone and corticotropin have not been useful, and in one case at least splenectomy was of no help. Radiation therapy or use of nitrogen mustard has been of doubtful value. However, in case 2, subsequent vigorous treatment with nitrogen mustard and triethylene melamine produced at least partial remission of symptoms and a significant decline in the amount of abnormal protein, according to follow-up information forwarded to us through the courtesy of Dr. Walter Rambach, Northwestern University Medical School, Chicago. It might be noted also that some subjective benefit occurred in case 4 after a course of nitrogen mustard given in the early part of the illness.

Summary

A study has been made of four cases of macroglobulinemia encountered at the Mayo Clinic. Macroglobulinemia should be considered as a syndrome, not as a disease entity. The main clinical features are mucosal bleeding, blurring of vision, lymphadenopathy, hepatosplenomegaly, and anemia. The cause is unknown.

Ultracentrifugation of the serum reveals large quantities of macroglobulins, which are globulins having Svedberg sedimentation constants of more than 15. The erythrocytic sedimentation rate is increased in almost every case, and exceptionally high blood viscosity is present. Hyperglobulinemia occurs, and serum electrophoresis shows a peak in the beta or gamma globulins. The bone marrow shows increased plasma cells and lymphocytes but is not diagnostic.

The ocular fundus in macroglobulinemia is distinctive, being similar to the picture in plasma cell (multiple) myeloma but with greater venous dilation. Scattered exudates and hemorrhagic zones are present. The prognosis is variable; some patients live for many years. Treatment is usually ineffective, but use of nitrogen mustard may give subjective improvement.

Ultracentrifugation in all four cases was performed in the department of Physiological Chemistry, University of Wisconsin, through the courtesy of Dr. H. F. Deutsch.

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ANTIPYRETIC EFFECTIVENESS OF SALICYLAMIDE AND ACETYLSALICYCLIC ACID IN INFANTS

A COMPARATIVE STUDY

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The course of fever was followed in a study of 512 pediatric patients whose initial temperatures were over 38.3 C (101 F) and whose physical findings justified an initial trial of antipyretic measures alone. The patients were treated on an alternating plan with either aspirin or salicylamide, for the purpose of comparing the effectiveness of the two drugs. The salicylamide sufficed in 110 patients, and only 39% of the salicylamide group required eventual treatment with antibiotics. The aspirin sufficed in 117 patients, and only 41% of the aspirin group ultimately needed antibiotics. The difference was not significant. Similar analyses of other quantitative aspects of the treatment revealed no significant differences in effectiveness between the two drugs. In ease of administration, acceptability to infants, and control of dosage, however, the salicylamide suspension had advantages over the form of aspirin used in this study.

Attempts have recently been made to discover or rediscover therapeutic agents which would possess the antipyretic and analgesic effects of acetylsalicylic acid (aspirin) without some of the undesirable attributes of this drug.[1] In the pediatric field two of these undesirable attributes are taste and the difficulty in preparing a stable liquid preparation for infants and small children who cannot take or who resist medicaments in tablet form. Adding flavors to acetylsalicylic acid inevitably raises the problem of tempting the youngster to regard the drug as a candy, with possible serious consequences through overindulgence. Tablets, of course, may be broken or crushed for administration, but in so doing accuracy of dosage is lost and one is still left with a gritty substance difficult to administer.

As a preliminary to this study, a series of blind acceptance observations were made on two substances, namely, salicylamide and N-acetyl-para-aminophenol, purporting to have clinical effects similar to that of acetylsalicylic acid. Various formulations of these two substances alone or in combination were tested on small infants. It eventually

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became apparent that the preparation (Liquiprin) containing salicylamide, as the active agent alone, was the more readily acceptable. Accordingly, this study was instituted to compare the relative antipyretic effects of salicylamide and acetylsalicylic acid. The selection of this particular action for study was obviously motivated by the fact that an objective appraisal of antipyretic effect is possible and much less liable to subjective error than, for example, the measurement of analgesic action. Furthermore, with the case material comprising, as it did, small infants, it was not possible to appraise analgesic effects. No definitive clinical study of the antipyretic effect of salicylamide appears in the literature.

Pharmacology

Chemically, salicylamide is 2-hydroxybenzamide and is not a true salicylate, since it does not have a free carboxyl group as does salicylic acid and acetylsalicylic acid. It is not hydrolyzed to salicylate, and, since the $CONH_2$ linkage is not easily broken, it should be less irritating than either free salicylic acid or sodium salicylate.[2] Salicylamide occurs as a white or slightly pink, crystalline powder, sparingly soluble in water at room temperature and soluble in oil, alcohol, ether, chloroform, acetone, and alkaline solutions. It is insoluble in petroleum ether and in carbon tetrachloride. In contrast to acetylsalicylic acid, it has little taste. Salicylamide is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout the body tissues.[2b] It is largely eliminated in the urine as the glycuronide. The effect of the drug on prothrombin time is debatable. Bavin and others[3] and Ichniowski and Hueper[4] conclude that it does not affect the prothrombin time, whereas Litter and others[5] claim that it shortens the prothrombin time.

In animal experiments as well as in some human studies, salicylamide appears to be productive of less toxic effects and greater tolerance than the salicylates, its LD_{50} being approximately twice that of aspirin.[6] This latter fact has an important clinical significance in that, in the unlikely event that an entire market package (50 cc.) were to be accidentally ingested by a child old enough to do so voluntarily, the probability of serious toxic effects would not be anticipated and, in any case, it would be far less than in a comparable situation involving aspirin.

Actually, if one can extrapolate from the observed LD_{50} for mice of 13 ml. per kilogram of body weight of the suspension, it is difficult to see how a child might ingest dangerous amounts. This would mean that a 3-year-old youngster weighing 14.5 kg. (32 lb.) would have to ingest the contents of more than three 50-cc. bottles in order to attain an LD_{50}, so even if the contents of one bottle were taken there would still exist a very wide margin of safety.

Clinical Material and Plan of Study

Clinical Material.—Infants and children in residence at the New York Foundling Hospital were incorporated in the study. This institution houses approximately 280 infants and children under 2 years of age, the majority of whom are under 1 year. Admissions are based on social need, since the Foundling Hospital serves as a repository for abandoned, dependent, and neglected infants. Qualified pediatricians make daily rounds throughout the institution, and night coverage is maintained by residents. While most of the infants are admitted as well infants, respiratory infections of the usual type are common, especially during the winter months. In addition, contagious diseases and febrile reactions to immunizations are not infrequent. Laboratory work, including x-rays, is available and forms a part of the routine medical care of these children.

Plan of Study.—Patients with temperatures over 101 F (38.3 C) and whose physical findings were such that it would appear that antipyretic measures alone would suffice to control the illness were treated on an alternating plan with either salicylamide or acetylsalicylic acid. Liquiprin, a suspension of salicylamide in a raspberry-flavored vehicle containing 64 mg. per cc., was administered by dropper. Spot checks of the droppers up to the measuring points indicated that they contained 0.9 cc. to 1.0 cc. For infants up to 6 months, from 6 months to 1 year, from 1 to 2 years, and from 2 to 3 years of age, dosages of 1, 2, 4, and 6 droppers (64, 128, 256, and 384 mg.) of the suspension of salicylamide or dosages of 32, 64, 128, and 192 mg. of aspirin, respectively, were given.

Suspension of salicylamide or aspirin was administered every four hours for temperatures over 101 F (38.3 C). In order that the study might not be unduly disturbing to small infants, temperatures were taken rectally, at the start, at 60 minutes and 120 minutes. If a satisfactory antipyretic effect was noted at 120 minutes, no further temperature records were taken until the time for the next dosage (four hours after the last). In cases where either no antipyretic effect was noted in 120 minutes or the temperature recorded was higher than at the start, the case was reevaluated and, if it seemed necessary, other forms of therapy were instituted. Because of this method of management, the cases could be divided into two main groups: in group 1 were those children who continued throughout their illness to take antipyretics alone and in group 2 were those who required, after a trial of antipyretic therapy, other supportive measures, most frequently antibiotics.

A further enumeration of data was made by recording individual trial periods. A trial period was the period of effect of a single dose of the antipyretic on temperature when no other supportive measures were utilized. This was measured from the time of determination of the initial temperature to that of the third determination 120 minutes later. Analysis of the trial periods was confined to group 1, since it was felt that, even though some infants received three or four doses of the antipyretic before other measures were introduced, these patients represented a different type of clinical material, with their illnesses having a variable bacterial etiology. No specific laboratory work was formally incorporated in the study since these infants, when ill, receive the usual laboratory examinations, blood cell counts, urinalyses, and x-rays as indicated.

Analysis of Results

Of the infants observed in this study, 19% were under 6 months old; 46% were from 6 to 12 months; 27% were from 1 to 2 years; and 8% were from 2 to 3 years. It will be noted that well over half (65%) were under one year of age and that there were very few over 2 years of age.

TABLE 1.—*Summary of Therapeutic Management with Salicylamide or Aspirin Alone and with Supplementary Therapy*

	Cases			Cases	
Type of Therapy	No.	% Total	Type of Therapy	No.	% Total
Group 1					
Salicylamide	110	42.9	Aspirin	117	45.7
Group 2					
Salicylamide and antibiotics	101	39.2	Aspirin and antibiotics	104	40.7
Salicylamide, antibiotics, and alcohol sponges	32	12.4	Aspirin, antibiotics, and alcohol sponges	29	11.3
Salicylamide and alcohol sponges	13	5.0	Aspirin and alcohol sponges	6	2.3
Total	256	...		256	...

A total of 512 patients were incorporated into the study (table 1). Of these, 110 patients were managed with salicylamide alone and 117 with aspirin alone. The remaining 285 ultimately required other forms of therapy to control their illnesses. Particular attention is also called to the distribution of the therapeutic management in group 2. The number of patients eventually placed on therapy with antibiotics was almost the same for the group receiving salicylamide (39.2%) as for those receiving aspirin (40.7%). The same relative findings are noted in the other forms of therapeutic management.

If one were to apply as the criteria for success or failure the ability of either drug to control fever without supplementary therapy, it is obvious from a study of table 1 that there would be little to choose between salicylamide and aspirin, since 42.9% of patients receiving salicylamide and 45.6% of those receiving aspirin required no other therapy. This apparent lack of difference may also be expressed by rearranging the data so that a comparison on the basis of success and failure may be made between the two forms of therapy. With salicylamide therapy there were 110 successes and 146 failures; with aspirin therapy there were 117 successes and 139 failures. The approximate chi-square value with one degree of freedom calculated from these data is 0.19. This is much smaller than the critical value of 3.84, which must necessarily be exceeded if the two drugs were to be considered different in their ability to control pyrexia.[7]

TABLE 2.—*Diagnosis of Patients in Group 1 and Number of Doses of Drug Given Before Pyrexia Was Controlled*

Doses, No.	Miscellaneous		Upper Respiratory Infection		Immunization		No Findings		Pharyngitis		Rhinitis		Mumps		Otitis Media	
	S*	A*	S	A	S	A	S	A	S	A	S	A	S	A	S	A
1	1	2	23	30	14	22	7	4	3	5	4	5	2	...	1	...
2	1	...	9	16	11	9	4	3	3	...	3	...	1	...	1	...
3	...	...	5	5	5	2	...	1	...	1	2	...	...	...	...	...
4	...	...	1	...	1	5	2	...	2	...	...	...	...	...	...	...
5	...	...	1	...	2	2	...	...	...	...	...	...	...	...	...	1
6	...	...	...	1	...	1	...	...	...	...	...	...	...	...	...	...
7	...	...	...	1	...	1	...	...	...	...	...	...	...	...	...	...
8	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
9	...	...	...	...	...	...	...	...	...	...	...	...	1	...	...	...
Totals	2	2	39	53	33	42	13	8	8	6	9	5	4	...	2	1

*S = salicylamide; A = aspirin.

While the above results are interesting from a clinical point of view, other measurements must be considered in a comparative evaluation of the two preparations. One of these is the number of doses required to control pyrexia. This could only be done without bias by utilizing the case material in group 1, where only salicylamide or aspirin was used. Table 2 records the diagnoses of the patients so treated and the number of doses needed to control the pyrexia. A study of the totals indicates that there was a fairly symmetrical spread of the various diagnoses between the two drugs.

TABLE 3.—*Number of Patients in Group 1 Classified According to Antipyretic Used and Number of Doses Required to Control Pyrexia*

Doses, No.	Salicylamide	Aspirin	Total
1	55	68	123
2	33	28	61
3	12	9	21
4-5	9	8	17
6-9	1	4	5
Total	110	117	227

Table 3 is a multinominal contingency table constructed from the data of table 2. It shows a comparison of the number of doses of salicylamide and aspirin needed to control pyrexia. The calculated chi square, with four degrees of freedom, is 4.34, the 5% critical value which should have been exceeded to show a difference is 9.49. This indicates, therefore, that there is no appreciable difference between the two drugs in the number of doses required to control pyrexia when either drug is utilized as the sole therapy.

Table 4.—*Temperatures, at Beginning of Trial Period, of 512 Patients, According to Antipyretic Used and Subsequent Supportive Therapy*

	Salicylamide				Aspirin			
Temperature, Fahrenheit	Without Supportive Therapy, No.	With Supportive Therapy, No.	Total	With Supportive Therapy, %	Without Supportive Therapy, No.	With Supportive Therapy, No.	Total	With Supportive Therapy, %
100.2-101.0	13	1	14	7.1	16	5	21	31.3
101.2-102.0	55	35	90	38.9	37	35	72	49.8
102.2-103.0	29	59	88	66.3	45	59	104	56.7
103.2-104.0	10	36	46	78.3	17	30	47	63.8
104.2-106.0	3	15	18	83.3	2	10	12	83.0
Totals	110	146	256	...	117	139	256	...

In table 4 the patients are grouped according to their initial temperatures and their subsequent management. It may be observed in this table that the percentage with support increases with the height of the initial temperature, regardless of the antipyretic used. The actual percentages have been superimposed on the regression lines in figure 1. It is apparent that with both drugs the need for added therapy increases in direct relationship to the height of the initial temperature. In the group with temperatures from 101.2 to 102.0 F (38.4 to 38.9 C), 90 were given salicylamide and 72 were given aspirin. In the group with temperatures from 102.2 to 103.0 F (38.9 to 39.5 C), 88 were given salicylamide and 104 aspirin.

The relationship that exists, from the data in table 4, between the proportion "p" requiring added support and the initial temperature "T" may be approximated by the following linear equations: 1. For salicylamide, $p=0.1717T-17.05$. 2. For aspirin, $p=0.0962T-9.33$. (A second degree equation may fit these data better, but only the slope is of interest here, and the first degree equation is adequate for this purpose.) The chi squares for the slopes with one degree of freedom are 36.2 and 10.3 for the salicylamide and aspirin equations respectively. The 5% critical value which must be exceeded to prove significance is 3.84. The analytical procedure involved is that suggested by Cochran.[8]

The plots of the equations are shown in the regression lines of figure 1. If these lines are really as different as the equations indicate, salicylamide will control pyrexia in a greater proportion of patients without supportive therapy than will aspirin when the "initial" temperature is less than 102.4 F (39.1 C); the converse is true when the temperature is above 102.4 F. A statistical comparison of the slopes of the two equations was made according to a procedure suggested by Connor.[9] The chi square for this comparison was found to be 3.33, with one degree of freedom, which exceeds 2.71, the 10% critical value, but fails to exceed 3.84, the 5% critical value. This analysis indicates only that there is a possibility that two different lines exist but that this has not been conclusively demonstrated.

In table 5, the 227 patients who were treated with antipyretics alone are grouped according to their temperatures at the start of their illnesses. As in the analysis of the combined groups (table 4), a significantly greater number of patients given salicylamide (61.82%) had starting temperatures under 102 F than did those given aspirin (45.3%). The same type of information has been determined in table 6, except that the grouping in this instance was based on the initial temperatures at each trial period. The percentage of patients given salicylamide, whose trial periods began at a temperature of 102 F or lower, was 56.3% and of those given aspirin 45.3%. The differences suggested by the two tables are statistically significant at the 5% level and indicate again that more of the patients with a high temperature received aspirin and more of the patients with a low temperature received salicylamide.

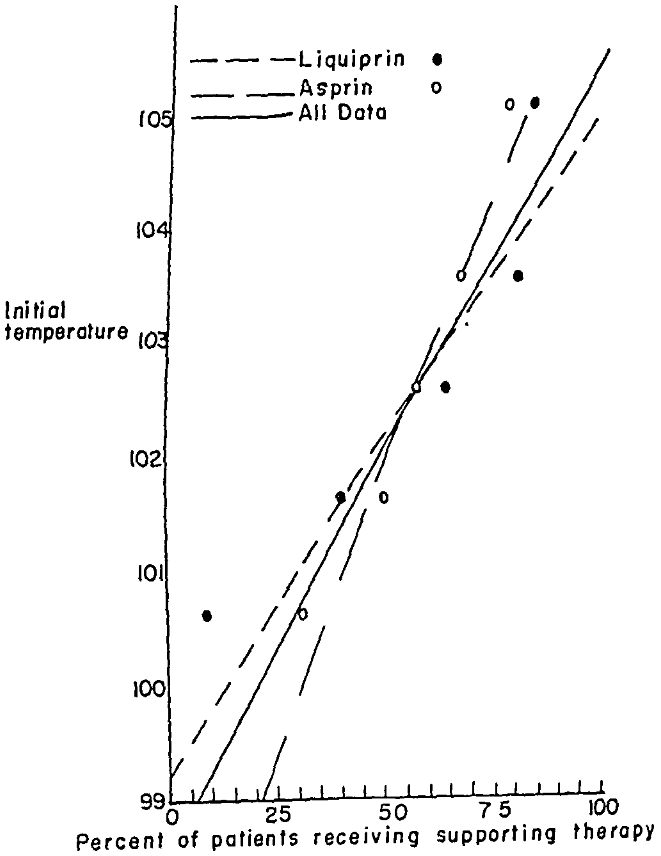

Fig. 1.—Regression lines showing percentage of patients requiring supportive therapy, as function of initial temperatures.

Figure 2 demonstrates the quantitative drops in temperature produced by the two drugs and the percentage of instances in which the drops occurred. Casual inspection of this graph would seem to indicate that aspirin produced greater drops in temperature than did salicylamide and produced these drops more frequently. Furthermore, failures, this is to say, either no drop in temperature or an increase in temperature, occurred more frequently with the salicylamide trials than with the aspirin. However, this conclusion is only suggestive and cannot be made with confidence Clinically, however, as was previously pointed out, aspirin was more frequently used in patients with higher temperatures than was salicylamide.

TABLE 5 —*Distribution of Patients in Group 1 According to Temperatures at Beginning of Illness*

	Patients Taking Salicylamide		Patients Taking Aspirin	
Temperature, Fahrenheit	No	%	No	%
101 0	13	11 82	16	13 68
101 2 102 0	55	50 00	37	31 62
102.2 103 0	29	26 36	45	38 46
103 2 104 0	10	9 09	17	14 53
104.2 105 0	3	2 73	2	1 71
Totals	110		117	

Throughout the course of this study, neither salicylamide nor aspirin produced any evidences of sensitivity or toxicity. There was little question, however, but that the suspension of salicylamide was more easily administered and more readily accepted by the infants

Comment

Emphasis should again be laid on the fact that all of the patients in this study presented no specific clinical findings on initial examination, save that of pyrexia. It is interesting, therefore, to observe that in this type of clinical material 42 3% of the patients could be controlled by antipyretics alone. This, of course, substantiates the opinion of many conservative physicians that the immediate introduction of antibiotics without clinical findings and on the basis of pyrexia alone is unwarranted Both drugs were equally able to control pyrexia in these cases without added therapy and with the same number of doses. As was pointed out, more than 42 9% of the patients who started on salicylamide therapy continued on treatment with that drug alone and 45.6% of those on aspirin therapy showed the same result.

TABLE 6 —*Distribution of Patients in Group 1 According to Temperatures at Beginning of each Trial Period*

	Patients Taking Salicylamide		Patients Taking Aspirin	
Temperature at Beginning of Trial Period, Fahrenheit	No	%	No	%
101 0	19	9 22	19	8 88
101 2 102 0	97	47 09	82	38 31
102 2 103 C	57	27 67	78	36 44
103 2 104 0	25	12 14	29	13 55
104.2 105 0	8	3 88	6	2 80
Totals	206		214	

The data seem to indicate that aspirin could produce greater drops in temperature and control pyrexia of higher degree than could salicylamide, but a qualitative difference between the two drugs could not be demonstrated conclusively. Further work would be needed to conclusively establish qualitative differences between the drugs A balancing of cases and an alternation of drugs on the basis of starting temperatures would provide this answer.

The symmetrical distribution of therapeutic management as demonstrated in table 1 is difficult to interpret. Indeed, until the final enumeration of data, this trend was unknown. It is true, however, that in the event of either antipyretic failing to stabilize the patient after three or four trials additive support was introduced.

Summary and Conclusions

A comparative study of the effectiveness of salicylamide (Liquiprin) and acetylsalicylic acid (aspirin) indicated that both drugs controlled pyrexia, in the absence of specific clinical findings, equally well and with the same number of doses. With both drugs, the need for additive supportive measures bore a direct relationship to the height of the temperature at the start of the illness. A qualitative difference between the two forms of therapy was not proved.

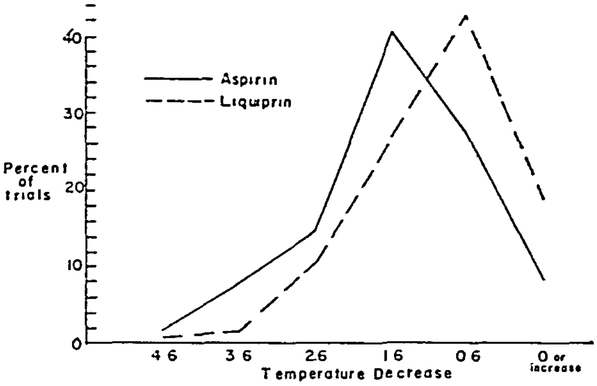

Fig 2 —Percentages of trials resulting in given temperature changes in patients in group 1.

In our experience, the salicylamide suspension proved superior to aspirin in ease of administration, better acceptability, and control of dosage. If one takes into consideration factors arising in nonprofessional nursing situations, the greater margin of safety of salicylamide must also be taken into account.[10] For these reasons, with the fact that no toxic reactions were encountered in our study, it was felt that the suspension offered definite advantages for use in young children

175 E. 68th St (21) (Dr Vignec).

This study was aided by a grant from the Research Division of Johnson & Johnson, New Brunswick, N J

The salicylamide suspension used in this study was supplied as Liquiprin by the Research Division of Johnson & Johnson, New Brunswick, N. J.

Dr. F. C Brenner made the statistical evaluation of the clinical data used in this study

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IMPROVED ACCURACY OF TES-TAPE IN ESTIMATING CONCENTRATIONS OF URINARY GLUCOSE

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Tes-Tape is an indicator paper used in the form of small strips to test urine for the presence of glucose. The enzyme on the paper, glucose oxidase, acts on the beta-form of D-glucose in the presence of oxygen to liberate hydrogen peroxide, which in turn oxidizes the ortho-tolidine on the paper to a blue pigment. Improved methods of manufacture have helped to prevent deterioration of the enzyme and to increase the accuracy of the color readings. In performing the test it is necessary to make sure that glucose is present in the beta-form and that oxygen is available. Additional precautions are essential, especially in testing urine heavily loaded with glucose. It is recommended that the user lay the strip flat against a white background for reading and that, if the one-minute reading indicates 0.5% (3+) glucose, a final reading be made at two minutes. The data here presented were obtained on both artificially made standard glucose solutions and naturally obtained specimens of diabetic urine. When used with due care, the Tes-Tape was both convenient and reliable for the semiquantitative estimation of urinary glucose.

The advent of Tes-Tape initially seemed to provide the most convenient method for estimating urinary glucose concentrations, since the indicator paper itself was the only material required. However, a few testimonials of its semiquantitative reliability [1] were inundated by other reports [2] alleging that the Tes-Tape color response often failed to distinguish between moderate and profound degrees of glycosuria. Our own data confirm the validity of the latter indictment.

This serious deficiency in performance clearly diminished Tes-Tape's value to the diabetic patient and his physician by reducing it essentially to a mere indicator of the presence of glucose. A systematic search was therefore conducted to find the reasons for erroneously low readings. Recognition and removal of multiple causes for underreading have resulted in an improved commercial product which fulfills its earlier promise to afford semiquantitative precision at least equal to that of older copper-reduction methods.

Technical Errors Causing Falsely Low Interpretations

Unpublished, yet unwarranted, criticisms of Tes-Tape's accuracy have sometimes stemmed from two errors in testing technique. The latter, in turn,

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were due to unfamiliarity with the reactions underlying the following Tes-Tape responses:

$$(1)\ \underset{\text{(in urine)}}{\text{Beta-D-glucose}} + \underset{\text{(in air)}}{\text{oxygen}} \xrightarrow[\text{(on Tes-Tape)}]{\text{glucose oxidase}} \text{gluconic acid} + \underset{\text{peroxide}}{\text{hydrogen}}$$

$$(2)\ \underset{\text{(on Tes-Tape)}}{\text{Ortho-tolidine}} + \underset{\text{peroxide}}{\text{hydrogen}} \xrightarrow[\text{(on Tes-Tape)}]{\text{peroxidase}} \underset{\text{(blue color)}}{\overset{\text{oxidized}}{\text{ortho-tolidine}}} + \text{water}$$

The critical quantitative factors are (1) an equilibrium state between the alpha and beta forms of D-glucose and (2) the availability of oxygen. Equilibrium is necessary because glucose oxidase reacts 150 times faster with beta-D-glucose than with the alpha isomer. This equilibrium exists in such aqueous solutions as voided urine. Anhydrous glucose, however, is primarily alpha-D-glucose, which requires about 30 minutes after dissolving to complete alpha-beta equilibration. For this reason, when standard solutions are made by dissolving dry glucose in sugar-free urine and testing immediately with Tes-Tape, low readings are always obtained. To illustrate, when 588 tests were performed by this technique, there was zero color response at concentrations of 0.1%, 0.25%, 0.5%, and 2.0% (representing 1+ to 4+ glycosuria) and only 9% correct readings with the 4.0% (4+) standard. When the same samples were retested 30 minutes later, the respective interpretations were 94%, 99%, 75%, 61%, and 71% correct.

The second procedural error has been committed by dropping a length of Tes-Tape into a urine sample and reading the color of the submerged strip a minute later.[3] Since oxygen is required for glucose oxidase to react with beta-D-glucose, low estimations are invariably obtained.

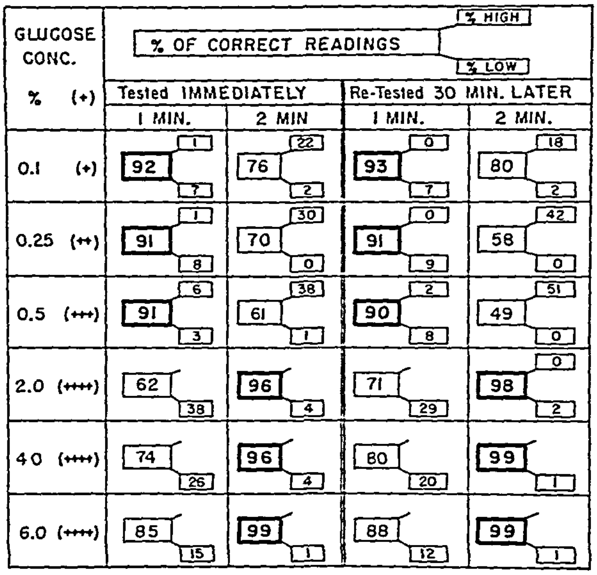
Neither of these technical artifacts contributed to published findings deprecating Tes-Tape's quantitative reliability. It was therefore imperative to duplicate the authors' testing methods when seeking the reasons for their poor results.

Materials and Methods

Data were obtained both on artificially constructed standard solutions and on spontaneous glycosuria. Test standards were made by adding aliquots of a 50% aqueous glucose solution to glucose-free urine and mixing by inversion. The stock 50% glucose solution was at least one day old. Respective glucose concentrations were 0.1%, 0.25%, 0.5%, 2.0%, 4.0%, and 6.0%. At each concentration, one to three observers did a total of 136 tests on 63 separate urine specimens. Eight different lots of Tes-Tape were used in performing 816 observations in this study.

A total of 2,947 individual Tes-Tape determinations were made on 249 specimens of urine voided by diabetic patients from 1 to 24 hours previously. Each sample was tested with five to seven different batches of Tes-Tape. Four of the lots were classified as "old Tes-Tape" and three as "new Tes-Tape," depending upon date of manufacture relative to the introduction in October, 1956, of improved methods for processing and packaging the material. Six observers participated in the study, with one to four workers testing each sample of urine. Each specimen was then quantitatively analyzed for "glucose" by Nelson's modification of the Somogyi method.[4] In addition, the precise glucose concentrations of 93 of these samples were simultaneously determined by a specific glucose-oxidase method (use of a quantitative glucose reagent [Glucostat]).

The following technique was used in estimating glucose concentration with Tes-Tape: A 1.5-in. strip of the material was dipped into the sample of urine and laid flat against a white background (glazed stationery). Saturation was such that the fluid front advanced slowly along the paper strip, but a dry portion always remained. After one minute of color development—the interval originally recommended by the manufacturer—the reading was made by comparing the area of most intense green-to-blue hue with the color chart on the Tes-Tape container. In addition, the Tes-Tape response was read again after two minutes of color development. Although most of the material tested was supplied by the manufacturer, three batches of "new Tes-Tape" were purchased from local pharmacies to evalute possible deterioration of the product during commercial handling.



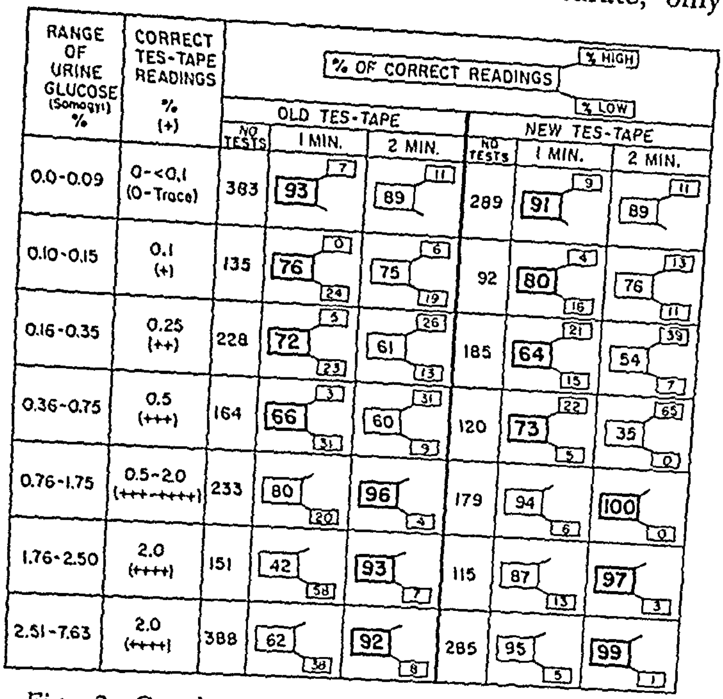
GLUCOSE CONC. % (+)	Tested IMMEDIATELY						Re-Tested 30 MIN. LATER					
	1 MIN.			2 MIN			1 MIN.			2 MIN.		
	% OF CORRECT READINGS	% HIGH	% LOW	% OF CORRECT READINGS	% HIGH	% LOW	% OF CORRECT READINGS	% HIGH	% LOW	% OF CORRECT READINGS	% HIGH	% LOW
0.1 (+)	**92**	1	7	76	22	2	**93**	0	7	80	18	2
0.25 (++)	**91**	1	8	70	30	0	**91**	0	9	58	42	0
0.5 (+++)	**91**	6	3	61	38	1	**90**	2	8	49	51	0
2.0 (++++)	62		38	**96**		4	71		29	**98**	0	2
4 0 (++++)	74		26	**96**		4	80		20	**99**		1
6.0 (++++)	85		15	**99**		1	88		12	**99**		1

Fig. 1.—Accuracy of Tes-Tape readings on standards made from 50% aqueous glucose solution added to sugar-free urine and tested both immediately and 30 minutes later.

Results and Comments

Tes-Tape Readings on Standard Glucose Solutions.—Two groups[4A] evaluated Tes-Tape by creating standards from stock 50% aqueous glucose solution and testing immediately, using the recommended reading time of one minute. In contrast to the findings on standards made up from dry glucose, findings on standards constructed from glucose already in solution were interpreted with equal accuracy by Tes-Tape both immediately and after a 30-minute latent period (fig. 1).

The paramount feature of the data in figure 1, however, was the sharp decline in correctness of one-minute readings at high glucose concentrations. Although the 0.1% (1+), 0.25% (2+), and 0.5% (3+) standards were 90 to 93% accurate, only 62 to 88% of the 2.0%, 4.0%, and 6.0% (4+) concentrations were correctly interpreted. These figures confirm previous reports of alarmingly low precision for glycosuria of 2.0% concentration or above (4+), since all such studies employed the recommended one-minute reading time. When an additional minute was allowed for maximal evolution of color, however, and the same Tes-Tape strips were read again at two minutes, 96 to 99% correct readings were obtained.



RANGE OF URINE GLUCOSE (Somogyi) %	CORRECT TES-TAPE READINGS % (+)	OLD TES-TAPE							NEW TES-TAPE						
		NO TESTS	1 MIN.			2 MIN.			NO TESTS	1 MIN.			2 MIN.		
			% OF CORRECT READINGS	% HIGH	% LOW	% OF CORRECT READINGS	% HIGH	% LOW		% OF CORRECT READINGS	% HIGH	% LOW	% OF CORRECT READINGS	% HIGH	% LOW
0.0-0.09	0-<0.1 (0-Trace)	383	93	7		89	11		289	91	9		89	11	
0.10-0.15	0.1 (+)	135	76	0	24	75	6	19	92	80	4	16	76	13	11
0.16-0.35	0.25 (++)	228	72	5	23	61	26	13	185	64	21	15	54	39	7
0.36-0.75	0.5 (+++)	164	66	3	31	60	31	9	120	73	22	5	35	65	0
0.76-1.75	0.5-2.0 (+++-++++)	233	80		20	96		4	179	94		6	100		0
1.76-2.50	2.0 (++++)	151	42		58	93		7	115	87		13	97		3
2.51-7.63	2.0 (++++)	388	62		38	92		8	285	95		5	99		1

Fig. 2.—Correlation between Tes-Tape estimation of spontaneous glycosuria and quantitative glucose determination (Somogyi).

Tes-Tape Interpretation Versus Actual Glucose Content of Urine.—More than two-thirds of all tests were done on urine voided by diabetic patients, in order to evaluate the crucial question of Tes-Tape's semiquantitative accuracy under the clinical conditions for which it was designed. Figure 2 shows that the product's ability to estimate spontaneous glycosuria was, on the whole, similar to its performance in detecting known amounts of glucose added to sugar-free urine (fig. 1). In both situations, one-minute readings were more accurate at lower concentrations, while two-minute readings were required to document high-grade concentrations. The apparently poor precision of one-minute readings at low concentrations in voided urine (fig. 2) is readily explained below and did not represent faulty Tes-Tape responsiveness.

Concerning the primary problem of Tes-Tape interpretations at high glucose concentrations, the one-minute readings with "old Tes-Tape" supported previous studies on voided urine,[5] which found the material deficient in detecting clinically hazardous degrees of glycosuria. Actual glucose contents from 1.76% to 7.63% were read as "2.0% or above (4+)" only 42 to 62% correctly, most of the faulty interpretations being hedged as "between 0.5% and 2.0% (3+ to 4+)." However, rereading after allowing two minutes for maximal color development magnified accuracy to 92 to 93%. Comparable testing with "new Tes-Tape" showed marked improvement at both reading intervals, with 87 to 95% precision at one minute and 97 to 99% correct quantitation at two minutes. All batches of "new Tes-Tape," whether obtained from the manufacturer or from commercial outlets, gave similar results.

The results in figure 2 seemed to expose a mediocre ability of Tes-Tape to interpret correctly glycosuria between 0.1% (1+) and 0.75% (3+) concentration. Even the more accurate one-minute readings were only 64 to 80% correct. This spurious "deficiency" of Tes-Tape was in fact due to its absolute specificity for detecting glucose alone.[6] By contrast, copper-reduction techniques like the Somogyi method used in this study to analyze urine specimens for "glucose content" also record as "glucose" small amounts of nonglucose reducing substances often present in urine. Fructose, galactose, pentoses, and salicylates exemplify such substances. When 93 urine specimens from diabetic patients were simultaneously analyzed by both the Somogyi method and a specific glucose-oxidase procedure (see table), respective values over the entire glycosuric range showed maximal differences from 0.10% to 0.47% of "glucose." Although these differences were inconsequential at high glucose concentrations, their magnitudes were evidence that at levels of 0.5% (3+) or below most of the apparently low Tes-Tape percentages shown in figure 2 were due to falsely high Somogyi values. Particularly striking in this respect were 40 additional urine specimens which were entirely negative to all seven batches of Tes-Tape but which contained "glucose" by the Somogyi method varying from 0.09% to 0.38%.

Urinary Glucose Estimation with Tes-Tape Compared to Quantitative Analysis by Copper-Reduction and Glucose-Oxidase Methods

Urine Specimens, No.	Tes-Tape Readings, %(+)	Range of Urinary Glucose Content, %		Urinary Content, %, of Nonglucose Reducing Agents, Range of A—B
		Copper-Reduction Method (A)	Glucose-Oxidase Method (B)	
28	0 (0)	0.09-0.18	0.00-0.05	0.08-0.16
13	0.1(+)	0.07-0.21	0.05-0.16	0.01-0.10
29	0.25(++)	0.16-0.61	0.13-0.39	—0.04-0.35
11	0.5(+++)	0.37-1.70	0.42-1.38	—0.03-0.39
12	2.0(++++)*	2.48-6.00	2.24-5.70	—0.07-0.47

* 2-min. reading.

Finally, with glycosuria of 0.5% (3+) concentration or less, the one-minute reading was more accurate than the two-minute reading because of a truly erroneous tendency for the color response to overdevelop into the next higher reading range during the second minute.

Comment

The present findings confirm the allegation that, under conditions employed in previous evaluations of Tes-Tape's semiquantitative reliability, the product frequently gave misleadingly low interpretations when high degrees of glycosuria actually existed. They show further, however, that minor modifications in reading technique, bolstered by technical improvements in the test material itself, now enable highly accurate estimation of glucose content at both low and high concentrations.

The former inability of Tes-Tape to distinguish between moderate (0.5% concentration, or 3+) and severe (2.0% and higher, or 4+) glycosuria was largely, but not entirely, the fault of the product itself. In descending order of importance, a combination of several factors accounted for the low readings:

1. The observer was originally instructed to read Tes-Tape after one minute of color development. Although this remains the optimum reading time for interpretations of 0.5% (3+) or below, two full minutes are often required for maximal color development signifying 2.0% or more (4+) concentration.

2. The importance of placing the Tes-Tape strip flat against a white background before reading was not appreciated previously. Instead of holding the strip in the air while reading, placing it on the porcelain washbowl or on the printing above the Tes-Tape color chart prevents light from diffusing through the tape and blanching an otherwise unequivocal 4+ color response.

3. Individual observers often read the same color response differently. In particular, an untrained person tends to hedge and make an intermediate reading (e. g., 2+ to 3+) if the area of darkest color development is not extensive, whereas the correct reading is usually the higher concentration (i. e., 3+).

4. When testing high glucose concentrations with "old Tes-Tape," confusion sometimes arose in interpreting the significance of the "intensity" versus the "hue" of color development.[2f] At concentrations of 2.0% or above (4+), although the tape developed a deep greenish-black color of much greater intensity than the 0.5% (3+) response, the final spectral change from dark green to dark blue pictured on the color card as the 4+ end-point sometimes failed to occur. This discrepancy between the end-point anticipated from the comparison chart and the actual hue appearing on the test strip understandably led to indecisive "between 0.5% and 2.0% (3+ to 4+)" interpretations.

5. As the material was formerly packaged ("old Tes-Tape"), exposure to excessively hot or humid environments promoted deterioration of the enzymes impregnated on Tes-Tape, with consequent reduction of its quantitative reliability.

Manufacturing improvements ("new Tes-Tape") introduced in October, 1956, have enhanced the analytical precision of the product by erasing the latter two causes for low readings. The spectrum of color development pictured on the reference chart on each dispenser is now matched more closely with the actual hues and intensities developed by the enclosed Tes-Tape. In addition, prompt packaging of the material after impregnation with the enzymes, together with individual foil-wrapping of each dispenser, minimizes deterioration from exposure to warm or moist conditions.

Notwithstanding these technical improvements, it is still advisable to incorporate two additional instructions for using Tes-Tape: 1. Before reading, the tape should be placed flat against a white background, e. g., above the color chart on the Tes-Tape dispenser itself. 2. If the interpretation at the one-minute interval is in the equivocal "0.5% to 2.0% (3+ to 4+)" range, a final reading should be made at two minutes in order to allow maximal color development. Although this maneuver sometimes results in over-reading actual 0.5% (3+) concentrations as 2.0% (4+), this slight inaccuracy is acceptable in practice because it does not alter clinical implications. The crucial fact is that clinically serious concentrations of 4+ are always recognized as such.

Summary and Conclusions

The semiquantitative accuracy of Tes-Tape in estimating all degrees of glycosuria was evaluated both by testing it on standard solutions of glucose in urine and by comparing the Tes-Tape reading with actual glucose content of urine from diabetic patients. Whether tested against contrived standard solutions or spontaneous glycosuria, Tes-Tape interpretations at the one-minute interval were highly reliable at concentrations of 0.5% (3+) or less, but were seriously inadequate in detecting glucose contents of 2.0% or more (4+). By allowing an additional minute for maximal color development, however, high-grade concentrations were detected with unimpeachable accuracy by both "old" and "new" batches of Tes-Tape.

Two additional instructions for using Tes-Tape are therefore strongly recommended: 1. The strip should be laid flat against a white background before reading. 2. If the one-minute reading is 0.5% (3+) or more, a final reading should be made at two minutes. It is concluded that Tes-Tape, when used as recommended, fulfills its original promise of providing the ultimate combination of convenience and reliability in the semiquantitative estimation of urinary glucose.

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This study was supported by a grant from Eli Lilly & Company, Indianapolis, who also provided most of the Tes-Tape.

Technical assistance was given by Mildred T. Brennan and Jean Dealy.

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CLINICAL NOTES

FEMOROPOPLITEAL ARTERIOVENOUS ANEURYSM CAUSED BY FRACTURED OSTEOCHONDROMA OF THE FEMUR

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Arteriovenous aneurysms of the extremities are usually caused by penetrating wounds (such as bullet or stab), but those due to a penetrating osteochondroma must be very rare. Paul[1] reported such a case in a 22-year-old man with multiple congenital osteochondromas, one of which penetrated the popliteal artery giving rise to an aneurysm with painful swelling of 17 days' duration. At the time of the operation, a pulsating hematoma or false aneurysm was found with a single hole in the popliteal artery. There was no venous involvement, and the artery was restored by suturing of the perforation. Paul reported that the dorsalis pedis and posterior tibial pulses did not return after surgery but that the patient was walking with ease.

Hudson[2] reported another case of a traumatic aneurysm in a 14-year-old boy with multiple osteochondromas. This patient gave a history of vigorous bicycling for two hours before sudden onset of pain in his left knee. An operation was performed after a preliminary attempt at immobilization for two weeks. Again, a single tear in the popliteal artery was found and repaired.

Report of a Case

The case reported here occurred in a boy, aged 14, who suffered a perforation at the femoropopliteal junction by an osteochondroma six years before we saw him. (We shall henceforth refer to this vessel as the femoral artery.) The patient reported that for the last few years his right lower leg had been markedly swollen and that during the last few months he had had considerable crampy pain, forcing him to stop on walking one block. He found it very difficult, or impossible, to participate in any physical activities at school. At the age of 8 he was once found on the floor in a fainting condition, complaining of severe pain in his right knee, and was seen by an orthopedic specialist. At that time he probably suffered a fracture of a cartilageous exostosis or osteochondroma with the fragment penetrating the artery and vein, causing formation of an arteriovenous fistula; the latter subsequently dilated into a true arteriovenous aneurysm.

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The boy was examined in consultation on Sept. 18, 1957. He appeared pale and was moderately well-developed for his age. His heart beat was 92 to 96 per minute, irregular, with numerous extrasystoles and a slight systolic murmur. Blood pressure was 120/68 mm. Hg. Chest x-rays were normal; the cardiac silhouette was not enlarged.[3] There was considerable swelling of the right leg. The calf was 3.5 cm. thicker and the lower leg about 1 cm. longer than the left,[4] and the skin over the right knee and leg felt warmer.[5] The right femoral pulse was pounding, but there was no right dorsalis pedis and no posterior tibial pulse palpable.

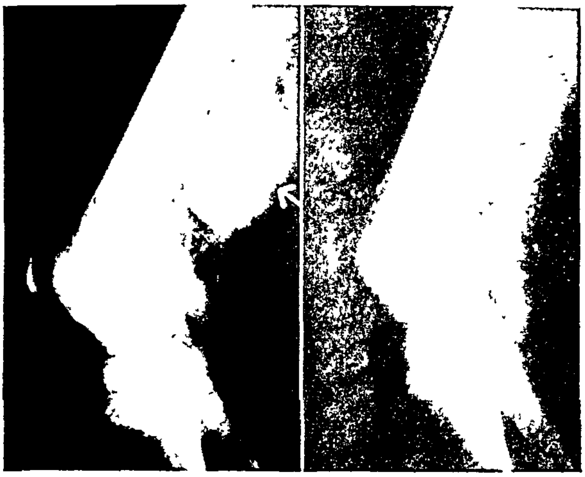

Fig. 1.—*Left,* femoral angiogram, outlining aneurysmal sac with fractured osteochondroma in center. *Right,* x-ray, taken March 27, 1958, five and one-half months after operation.

A pulsating mass was found on the inside of the right leg above the knee, measuring 15 by 10 cm. in diameter. It was only partly compressible, and a marked systolic and diastolic thrill and bruit was audible on direct auscultation over the mass and along the femoral artery. The thrill and bruit could be stopped by compression of the artery above the aneurysm, a phenomenon already described by Hunter [6] in 1757. This compression also resulted in slowing of the pulse rate (Nicoladoni [7]-Branham [8] sign, or Matas' bradycardiac reaction).[9] A femoral angiogram confirmed the diagnosis of an aneurysm and showed a fractured osteochondroma protruding into its center (fig. 1, *left*). X-ray bone survey revealed no other bone spur, although osteochondromas are usually multiple. An operation was performed by one of us (A. J. L.) on Oct. 19. A 12-in. incision was made over the medial lower part of the right thigh with an L-shaped extension toward the fossa poplitea. The aneurysmal sac was carefully dissected off the sartorius and adductor muscles and medial femoral and popliteal nerves. The femoral artery was exposed above Hunter's canal and was secured with tape and a bulldog clamp. The popliteal artery below the aneurysm was treated in a similar manner. Thus, the main arterial blood supply to the aneurysm was controlled. The aneurysm was then completely dissected and was entered through an opening close to its venous drainage. The sac was carefully removed off the vein and artery, leaving a 1-cm. round defect in the markedly dilated popliteal vein and a 4-cm. gap between the arterial stumps (fig. 2, *top*).

In view of the youth of the patient and the known drawbacks of all grafts, i. e., inability to grow and late thrombosis, we preferred to restore the 4-cm. arterial defect by a primary anastomosis. To obtain more length for bridging the gap, the proximal stump of the artery was mobilized and collaterals were cut and ligated. No extensive mobilization was done on the distal segment. After bending the knee 25 degrees, it was possible to approximate the two arterial stumps [10]—measuring only 4 mm. in diameter—with fine 00000 vascular oiled silk suture placed continuously on the posterior wall and interrupted anteriorly. The lateral defect in the vein wall was readily closed with adjacent sac wall. Ten mg. of heparin was used repeatedly for local irrigations. After release of the bulldog clamps, a good pulse beyond the anastomosis was noticed. The bone spur, which penetrated to the center of the cavity of the aneurysm, was then removed, and the bone was smoothed with chisel and file.

After wound closure the knee was immobilized in flexion on a well-padded plaster splint; it was gradually extended during the next few weeks. The patient had a good dorsalis pedis and posterior tibial pulse immediately after the operation and thereafter. Postoperative treatment consisted of antibiotics and 25 mg. of heparin given subcutaneously and 1 Gm. of aspirin every eight hours. The opened aneurysmal sac showed blood clots and two arterial and one main venous opening (fig. 2, *bottom*). Histological examination of the sac wall revealed remnants of the internal elastic membrane, proving the derivation of the sac from the arterial wall and confirming the true nature of its origin (fig. 3).

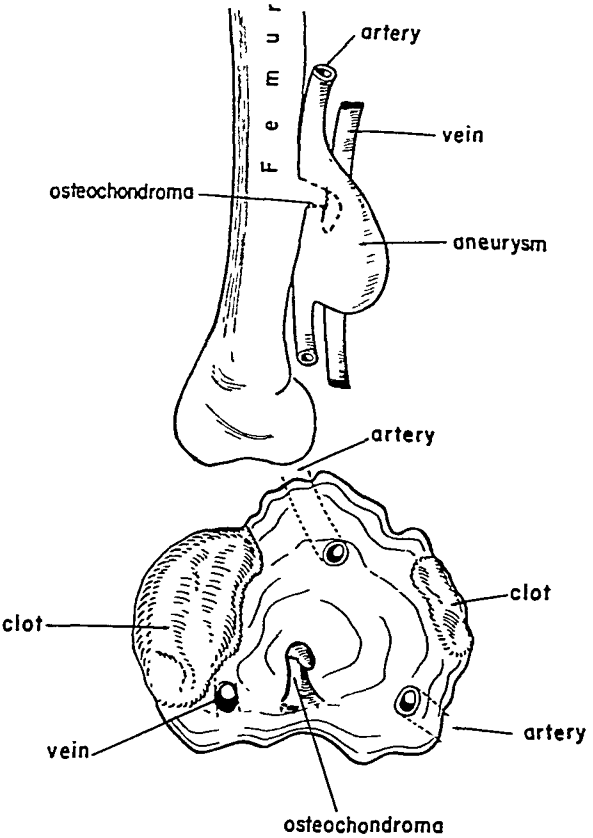

Fig. 2.—*Top,* schematic drawing of arteriovenous aneurysm 15 by 10 cm. in diameter. *Bottom,* schematic drawing of aneurysmal sac opened.

The boy returned to school on crutches three weeks after surgery. Three months later his knee was completely extended, and he walked well without any support. The right calf appeared to be decreasing in thickness, and there was hardly any subcutaneous edema. X-ray reexamination five and one-half months later revealed normal bone structure (fig. 1, *right*).

Comment

This case seems to be unusual in two respects. Unlike the two other patients described in the literature, our patient showed only a single osteochondroma and a true aneurysm. The history would indicate that this youngster sustained trauma at the age of 8, at which time a preexisting osteochondroma with the cartilagenous cap penetrated the adjacent femoral artery and vein and gave rise to an arteriovenous fistula. Gradually the arteriovenous fistula grew and developed into a fist-sized aneurysmal sac, causing the described disability.

At time of the operation, the problem of restoration of the venous defect was solved by closing the lateral perforation in the vein wall with adjacent aneurysmal wall tissue. However, the problem of arterial restoration was complicated by the small caliber of the vessel (4 mm.) and by the distance of 4 cm. between the two stumps to be bridged. In view of the fact that we were dealing with a growing patient, we felt that any replacement with homograft or nylon tube might lead to a relative narrowing or possible thrombosis of this area. Therefore we resorted to mobilization of the proximal stump and flexion of the knee to facilitate approximation.

No collaterals were sacrificed on the distal stump, but several collaterals were ligated proximally. This not only permitted a lengthening of the proximal stump but also increased the thrust across the anastomosis, which is considered an added safeguard against secondary thrombosis. It may also be worth mentioning that the anterior half of the anastomotic suture line was made with interrupted sutures to allow for widening of the vessel during growth. The gradual extension of the knee after the operation was tolerated without any interference with circulation.

Summary

Intermittent claudication in a 14-year-old boy was due to a traumatic femoropopliteal arteriovenous aneurysm caused by a penetrating fractured osteochondroma. Resection and end-to-end anastomosis of the artery and repair of the vein completely restored circulation and function.

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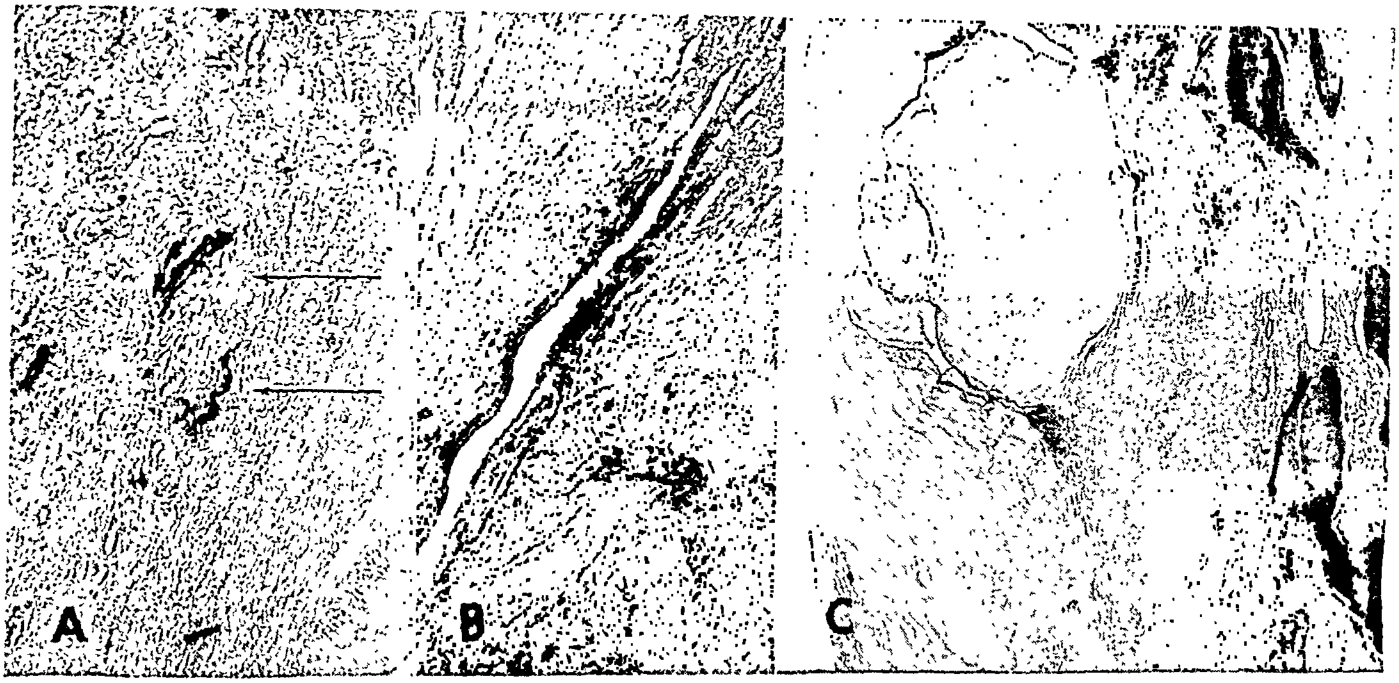

Fig. 3.—*A*, wall of aneurysm with laminated internal elastic membrane (indicated by arrows), stained with Verhoeff's elastic stain (× 40). *B*, bony tissue from osteochondroma and wall of aneurysm in left upper corner (× 40). *C*, cartilagenous cap of osteochondroma (× 40).

The authors wish to acknowledge technical assistance by the departments of pathology of Cedars of Lebanon, Temple, and North Hollywood hospitals and by Drs. W. Miller and J. Fields.

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ENURESIS DUE TO URETERAL ECTOPIA

REPORT OF A CASE

William H. Cooner, M.D., Harry M. Burros, M.D.
and
Eduardo Canon, M.D., Philadelphia

This case report is presented in order to emphasize the necessity of careful and complete evaluation of the urinary tract of children with the complaint of enuresis. While most often this problem resolves itself into one of psychogenic origin, this diagnosis must not be made until organic etiology has been ruled out. One of the frequent causes of this symptom in the female is ureteral ectopia, the diagnosis of which may be so elusive as to require prolonged, persistent effort before it can be demonstrated.

Grieve and Thomson[1] report a case of bilateral renal duplication with incontinence and provide a review of the literature pertaining to this condition. Campbell[2] gives the over-all incidence of ureteral ectopia, as determined from autopsies of children, as about 1 in 1,900, occurring three to four times as often in females as in males. Since the ectopic orifice always lies superior to sphincteric control in the male, incontinence does not result, however, in about 50% of females with an ectopic orifice, the opening is external to the sphincter, with resulting incontinence.

This 5-year-old child was first seen in May, 1955, because of "leakage of urine." The mother stated that the patient was well toilet-trained at the age of one year and that there had been no symptoms referable to the urinary tract until four months prior to her presentation at the clinic. At that time, she began to wet the bed consistently at night, even though she was aroused several times during the night to void. She also dribbled urine during the daytime, especially when she sneezed or coughed or was scolded by the mother. The child's parents had separated about the time these symptoms began, and the mother related their onset to the stressful home situation. There was no history of burning on urination, hematuria, or urgency.

Physical examination revealed no significant abnormalities. There was a moderate anemia, with hemoglobin level of 10.5 Gm.%. Urinalysis revealed 2-5 white blood cells per high-power field, and urine culture was reported as showing Staphylococcus aureus. Cystoscopy revealed no evidence of inflammation, stone, or other pathological process. Both ureteral orifices were visualized and were normal in position, size, and configuration. No ectopic ureteral orifice was seen. Cystometrogram yielded an essentially normal curve. It was

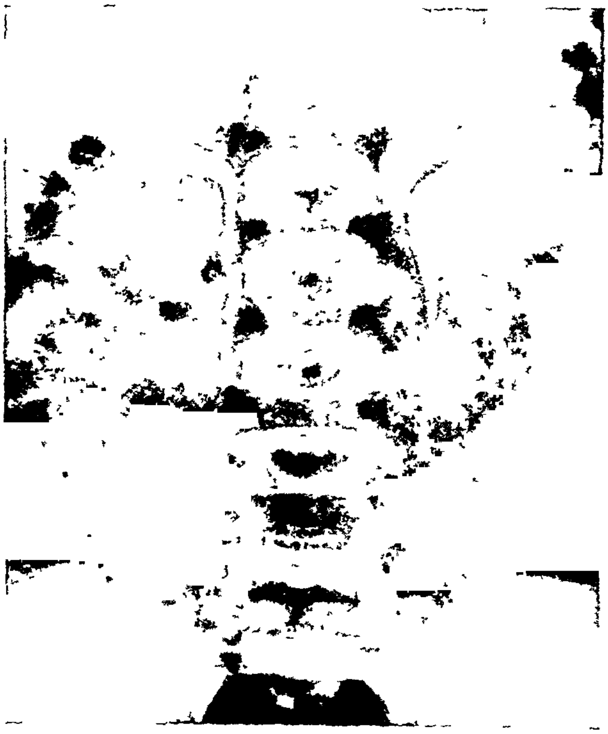

Fig. 1.—Urogram showing apparently normal right upper urinary tract and reduplication of left kidney calyces and pelvis.

From the Department of Urology, the Graduate Hospital of the University of Pennsylvania and the Graduate School of Medicine of the University of Pennsylvania. Dr. Canon is now at the University of Cali, Cali, Colombia.

felt that no organic pathological process existed to account for the patient's symptoms, and she was discharged with the diagnosis, "urinary incontinence secondary to psychogenic factor."

She was asked to return to the clinic in one year, and did so, at which time she was found to have almost constant dribbling, in addition to apparently normal acts of voiding. Physical findings this time were essentially the same as before. The hemoglobin level had risen to 12 Gm.%, and urinalysis was again unremarkable. Careful observation of the voiding pattern revealed almost constant dribbling, but with interspersed episodes of normal voiding. Excretory urography (fig. 1) showed an apparently normal right upper urinary tract, and reduplication of the left kidney calyces and pelvis, and probably also of the ureter. Armed with this information, another search for an ectopic ureteral orifice was undertaken. Close inspection revealed a small opening just posterior to the urethra (fig. 2). A 4 F. ureteral catheter was passed into this opening a distance of 6 cm., beyond which it could not be passed. Intravenous injection of sodium indigotindisulfonate (indigo carmine) showed this to be a ureteral opening. Retrograde injection of contrast material revealed the ureter to be markedly dilated and associated with the upper renal segment on the left side (fig. 3).

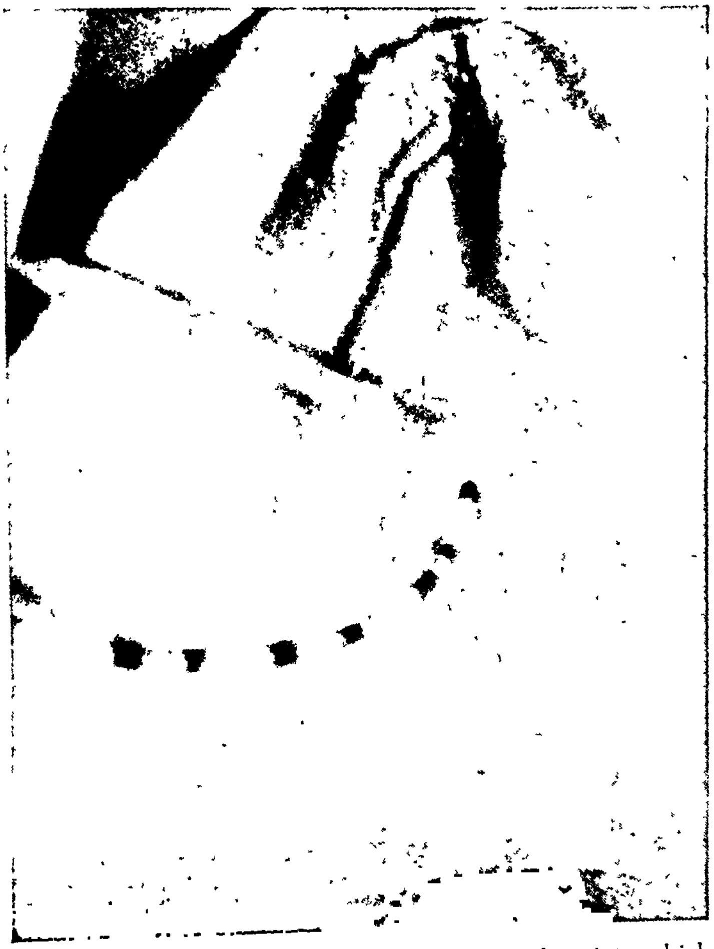

Fig. 2.—Small opening just posterior to urethra, into which 4 F. catheter was passed.

Exploration was performed through a left flank incision. Two ureters were identified, the one to the superior segment being markedly dilated. This segment and as much of the ureter as possible were removed. The postoperative course was uncomplicated. The patient left the hospital one week later and has since voided normally.

Comment

Development of an ectopic orifice is thought to depend on communication between a remnant of the mesonephric (Wolffian) duct, which becomes Gartner's duct in the female, and the vagina, cervix, or uterus. This communication may exist at birth or may develop after several years on perforation of a cyst in Gartner's duct.

Intravenous urography may fail to make one suspect an ectopic ureter if the function of the renal segment involved is so impaired as to prevent adequate excretion of contrast material. In addition, cystoscopy may reveal nothing abnormal, since two normally situated ureteral orifices may be identifiable. Retrograde pyelography carried out through the normal ureteral orifice may be helpful if the calyceal pattern suggests missing calyces (usually the superior). Use of orally or intravenously administered dyes is frequently most helpful, and use of this technique early in the course of the investigation will often permit identification of the ectopic orifice much sooner than by any other method.

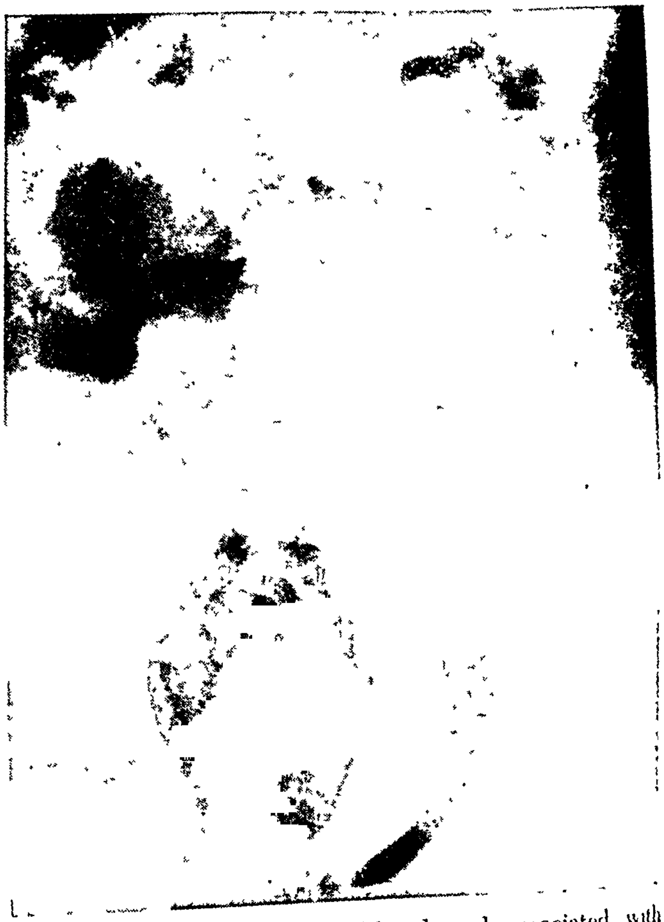

Fig. 3.—Ureter markedly dilated and associated with upper renal segment on left side.

Summary

This case of ureteral ectopia, with resulting incontinence, emphasizes the importance of complete evaluation of the urinary tract of children with enuresis. The use of orally or intravenously administered dyes as an aid in locating an ectopic orifice is frequently the preferred diagnostic technique, as other commonly used studies are often not helpful in revealing this abnormality.

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SEVERE REACTION TO METHOXAMINE HYDROCHLORIDE

REPORT OF A CASE OCCURRING DURING TREATMENT OF PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA

J. Richard Durham, M.D., Wilmington, Del.

Since Nathanson and Miller[1] first reported on the action of methoxamine (Vasoxyl) hydrochloride in the treatment of paroxysmal supraventricular tachycardia in 1952, several reports in subsequent years have suggested that this drug might prove to be the best agent for terminating this common arrhythmia after the usual simple measures to stimulate the vagus have failed. The drug is a synthetic sympathomimetic amine compound which differs from epinephrine mainly in having a methoxy instead of a hydroxy group on the benzine ring. The chemical designation is β-hydroxy-β-(2,5-dimethoxyphenyl) isopropylamine hydrochloride.

This drug will not induce ventricular fibrillation or other arrhythmias as epinephrine does, even in the cyclopropane-sensitized heart; it does not prevent carotid sinus–induced cardiac standstill, nor does it increase the ventricular rate in heart block. The bradycardia caused by intravenous injection can be abolished or prevented by atropine, which is, therefore, the antidote.

Lahti and associates[2] reported that methoxamine in overdosage (in dogs) caused sinus pauses and short runs of atrioventricular nodal rhythm. With lethal doses, death resulted from respiratory arrest and the heart action remained satisfactory. The mechanism of action in terminating the tachycardia is believed to be due to a rise in pressure in the arteries which activate all four afferent pathways concerned with cardiac slowing—that is, the baroceptors in the carotid sinuses and the aortic arch. Aviado and Wnuck[3] believe that, in addition to the constrictor action of the drug on systemic vessels, stretch receptors in the cardiac wall may be acted on by the drug. No direct proof of the latter action was offered, however.

Nathanson and Miller[1] reported a dull headache with intravenous doses of 4 to 5 mg.; sometimes a fulness in the chest or a prickly sensation was noted. This did not seem severe, and no acute apprehension, palpitations, or throbbing in the neck were complained of, such as are often seen with epinephrine in pressor doses. These authors recommended 8-10 mg. given intravenously as a usual dose and reported two cases in which the attacks ended within a minute after the injection.

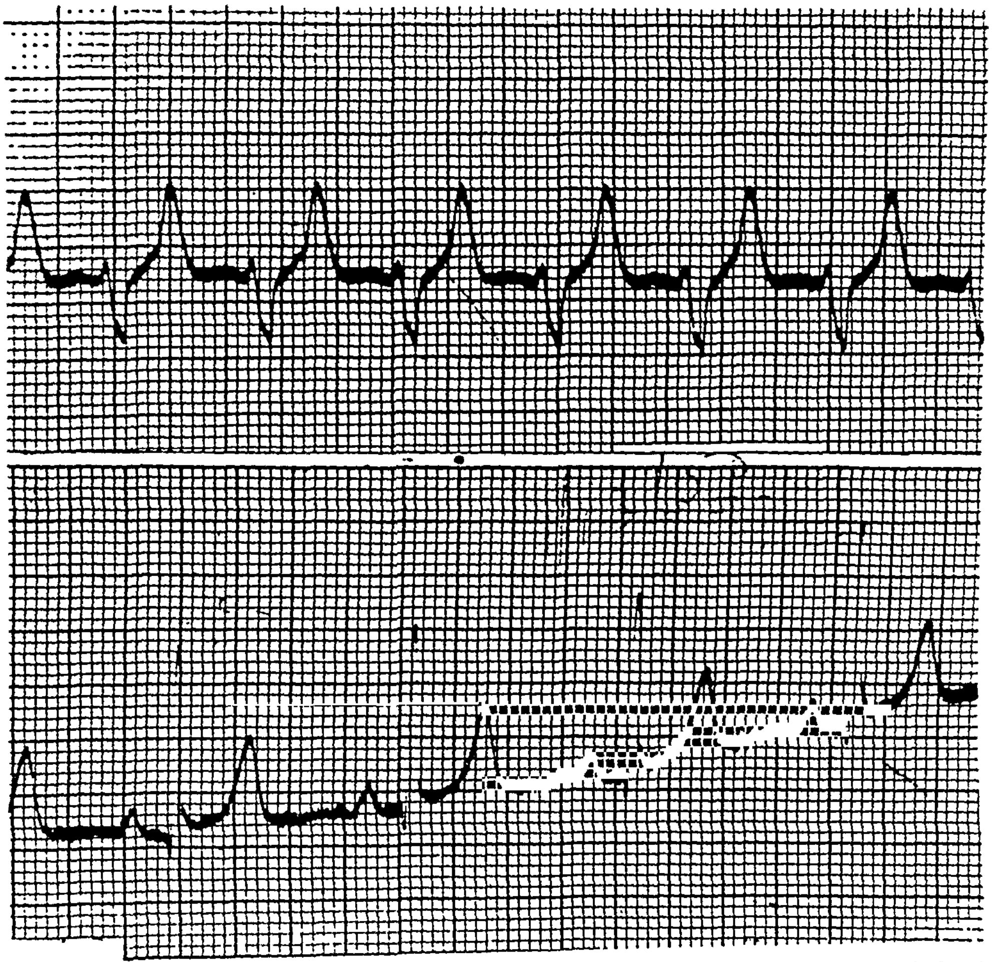
Subsequently, Berger and Rackliffe[4] reported two cases, in 1953, in which paroxysmal tachycardia was quickly terminated by methoxamine administration without side-effects. They pointed out the value of the drug in combating the frequently accompanying vascular shock.

In 1954, Chotkowski and co-workers[5] reported three cases of supraventricular tachycardia which responded quickly to the administration of methoxamine, usually in 10-mg. doses, sometimes repeated. Weakness and nausea were noted at times, but these were of slight degree and not incapacitating.

Since these reports, methoxamine has been used quite frequently for the cessation of this particular arrhythmia. In the past two years, I have employed the drug in office or home treatment without side-effects in 12 cases. Occasionally, a second intravenous dose of 10 to 20 mg. has been required. It has been my practice to use the 20-mg. ampul undiluted, giving the drug very slowly by vein and having the stethoscope over the precordium while the injection is being made. Frequently, the tachycardia ceases prior to the emptying of the syringe. Usually about 10 mg. is sufficient to cause conversion. On two occasions, 20 mg. in separate injections about 10 minutes apart was required; in one of these, carotid sinus pressure was effective after the second injection was completed, suggesting that methoxamine reinforced the effect of pressure on the sinus.

Report of a Case

A 39-year-old woman was known to be subject to bouts of a disturbing, regular, but relatively slow tachycardia since 1946, although such attacks were not documented by electrocardiogram until July, 1953. It will be noted in the tracing (see figure) that the tachycardia reveals an aberrant ventricular conduction with a rate of 110. The chest leads (not shown) revealed a late instrinsic deflection over the left side of the heart, and the pattern was considered to be indicative of a supraventricular tachycardia with an abnormal conduction simulating a left bundle branch block pattern. This particular attack was suddenly converted by subcutaneous administration of neostigmine (Prostigmin) bromide followed by carotid sinus pressure. There was no demonstrable organic heart disease on auscultation or fluoroscopic study. The patient was of slender habitus, her weight averaging 105 lb. (47.6 kg.).



Electrocardiographic tracing showing (*above*) paroxysmal tachycardia and (*below*) immediate return to sinus rhythm after neostigmine administration and carotid sinus pressure.

Because of the frequency of these attacks, various prophylactic programs were attempted, with use of quinidine sulfate, procainamide (Pronestyl) hydrochloride, and digitalis. None of these drugs in full dosage prevented the attacks from breaking through, and the patient eventually became sensitive to quinidine. By November, 1957, the attacks were occurring about every 10 days and were accompanied by considerable anxiety. This frequently necessitated the use of meperidine (Demerol) hydrochloride, 100 mg. given subcutaneously, plus barbiturates for sedation. With this treatment, the attack usually subsided during sleep.

The patient presented herself in the office on Dec. 20, 1957, having experienced a bout of tachycardia which had been present for the last 14 hours. Again, the usual measures failed to convert the rhythm, and on this occasion administration of one ampul of methoxamine, containing 20 mg., was started intravenously, undiluted. After about 10 mg. had been administered, the rhythm suddenly reverted to slow normal sinus rhythm, with a rate of about 64, confirmed by electrocardiogram monitoring. The needle was withdrawn, and the patient suddenly screamed because of an excruciating, almost unbearable headache. This was accompanied by projectile vomiting, and 200 mg. of meperidine was immediately administered to allay the pain. Her blood pressure prior to methoxamine administration had been 90/60 mm. Hg, and its highest point after administration was only 140/90 mm. Hg. This seemed insufficient to cause such an excruciating headache, and the possibility of some congenital abnormality of the cerebral circulation (cerebral aneurysm) came to mind. After about one hour, the headache, which was described as a severe band encircling the scalp, subsided to the extent that the patient was able to sit up in a chair. The rhythm remained normal, and the nausea and vomiting gradually subsided.

Comment

Salomon[6] reported a refractory case in which there were rather marked side-reactions to a single dose of 20 mg. of methoxamine, with "intense headache, general nervousness . . . accompanied by rectal and vesical tenesmus," lasting for one hour. Despite what was possibly an unnecessarily large dose, the tachycardia recurred two and one-half hours later. Elek and associates[7] also reported a case in which recurrence of the tachycardia followed two minutes after 6 mg. of methoxamine had converted the arrhythmia; possibly this dose was too small.

My patient's reaction, in connection with Salomon's report, would seem severe enough to cause questioning the use of methoxamine as part of a routine home treatment for supraventricular tachycardia. However, I have continued to use it, both in office and in home treatments, for attacks of paroxysmal tachycardia but have taken the precaution to have atropine available in case of a severe reaction.

No attempt has been made to review the voluminous literature on the numerous methods for terminating paroxysmal tachycardia. Briefly, it is my practice to instruct the patient suffering from this common arrhythmia in the usual simple measures to stop the attack: carotid sinus pressure, Valsalva maneuver in head-down position, iced drinks, and induced vomiting. If these fail, quinidine in doses of 0.6 to 0.8 Gm., followed by 0.4 Gm. every half hour, for three or four doses, is tried. If this is ineffective, further therapy by the physician is indicated. Prophylactic therapy is not recommended unless the attacks occur frequently enough to justify the nuisance of daily medication. This usually means weekly or biweekly attacks.

It is my feeling that methoxamine should still be considered as perhaps the best drug for the termination of these attacks, provided that the physiological antagonist, atropine, is at hand and provided that the drug is given slowly in a dose of 10 mg. Possibly, in individuals of slight habitus, such as was the case here, it might be well to dilute the drug in a few cubic centimeters of isotonic sodium chloride solution.

Summary

A severe reaction to methoxamine hydrochloride occurred during its use in the treatment of paroxysmal supraventricular tachycardia. Despite this reaction, the drug may still be the best medicament for routine office and home use in the treatment of this usually benign arrhythmia.

Addendum

Since submission of this article, I have had an opportunity to treat a 20-year-old college student with paroxysmal tachycardia and a Wolff-Parkinson-White syndrome known to be present since childhood. The patient had experienced the tachycardia for about five hours; an electrocardiogram revealed a supraventricular tachycardia with the aberrant QRS complexes so frequently seen in patients with this syndrome. The rate was 212 per minute. Previous attacks had been stopped by various combinations of neostigmine, lanatoside C (Cedilanid), the Valsalva maneuver, and carotid sinus pressure.

A 20-mg. ampul of methoxamine was placed in a syringe undiluted and administration started slowly by vein, with the patient in the recumbent position. It occurred to me that any unpleasant reaction might be avoided by asking the patient to state whether she felt tingling and to what extent. Therefore, the rate of injection was controlled by the amount of tingling which she experienced. At the same time, the patient performed the Valsalva maneuver intermittently. After 12 mg. of the drug had been introduced in approximately two minutes' time, the rhythm suddenly converted to a slow normal sinus rate. A post-tachycardial tracing revealed typical complexes of the Wolff-Parkinson-White syndrome.

While atropine should be kept on hand, it is now felt that any severe reaction can usually be avoided by slowing or momentarily stopping the injection as the patient's tingling sensation increases.

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PROGNOSIS OF PERNICIOUS ANEMIA.—Until Minot and Murphy introduced, in August 1926, the special diet therapy for pernicious anemia, treatment for this condition had been unsatisfactory. The diet was especially rich in complete protein and iron, particularly liver. It was soon observed that except for those with marked disorders due to spinal cord degeneration, all patients who observed this diet showed marked symptomatic improvement and a prompt, rapid and distinct remission of their anemia. Before the discovery of the beneficial effects of whole liver in pernicious anemia, the life expectancy of the patients with this disease was considered to be short, often a few months or years at least. There has now been more than 30 years of experience in treating patients with pernicious anemia, first with whole liver, later with liver extracts and vitamin B_{12} as substitutes for liver. With closer contacts between patients and physician for proper guidance of therapy, we find such patients live long and useful lives, often exceeding that of other members of their age group.—S. D. Conklin, M.D., Report of a Case of Pernicious Anemia Under Treatment for 31 Years, *The Guthrie Clinic Bulletin,* April, 1958.

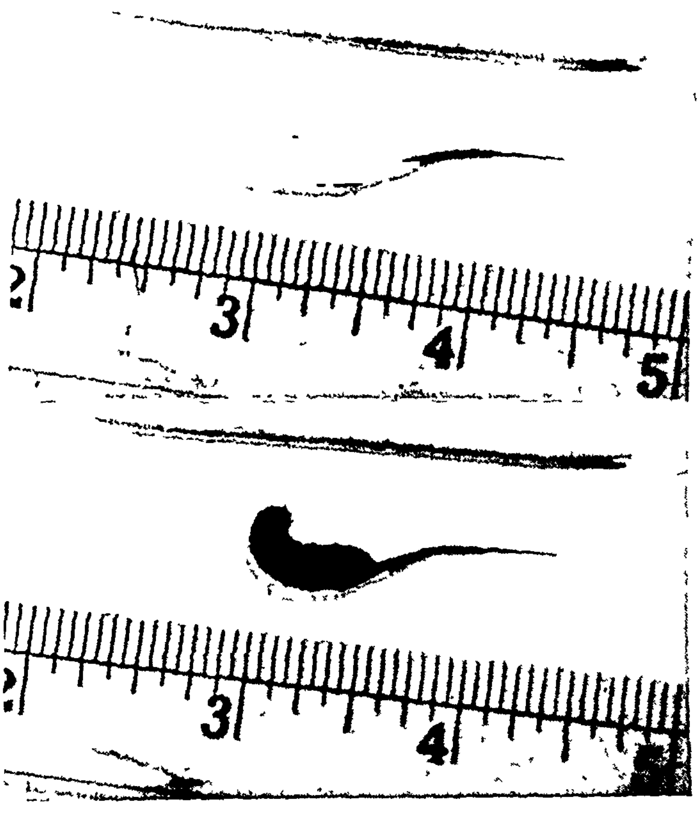
GENITOURINARY MYIASIS DUE TO ERISTALIS TENAX

REPORT OF A CASE

Charles J. Supple, M.D., Toledo, Ill.

A 16-year-old patient was delivered of a term infant on May 2, 1957, after an uneventful pregnancy and labor. Urinalyses were consistently negative, blood pressures were normal, ankle edema was absent, and a Kahn test and chest x-ray were negative.

About one week after delivery the patient started to complain of intermittent and colicky pain in the left lower quadrant, anorexia, nausea, occasional vomiting, chronic fatigue, and gradual loss of about 10 lb. (4.5 kg.). The parents are well-to-do, fastidious farmers who exercise care about personal habits and cleanliness. Pelvic examination revealed normal postpartum findings; urinalysis was negative. One month after the onset of these symptoms the patient passed spontaneously in her urine an organism (see figure) identified as a rat-tailed maggot.[1] The size was about 3.5 cm. in length and 0.7 cm. in diameter, and the tail measured 4.5 cm. in length. The next day another organism was passed. The patient was given hexylresorcinol (Caprokol), 1 Gm. in one dose, followed by epsom salts catharsis 24 hours later. No organisms were passed per anus or urethra. The patient's course changed. She ate better, the pain left completely, and she has been asymptomatic with no recurrence since.



Rat-tailed maggots passed in urine of patient one month after onset of symptoms.

Comment

The diagnosis of Eristalis tenax was confirmed by submitting the specimen to the Armed Forces Institute of Pathology[2] and to Dr. Carroll Birch of the University of Illinois College of Medicine, department of parasitology.[3] The organism is characterized by an anal breathing tube and usually hangs downward from the surface of water.[4] The adult is a large fly but resembles a drone bee.[5]

DeGroot,[5] in 1956, divided maggots into four groups. The first group included the blood-sucking ones, such as Auchmeromyia luteola, found in South Africa. The second group included the wound and natural cavity invaders. These can actually clean wounds and are of the genera Calliphora, Sarcophaga, and Wohlfahrtia. The invaders of the gastrointestinal and genitourinary tracts are in the third group and are very rare. The fourth group may penetrate the skin and cause boils or the creeping eruption (larva migrans) of the skin of infants, as seen in the southern states.[5]

A perusal of the Quarterly Cumulative Index Medicus reveals no mention of E. tenax as a cause of genitourinary myiasis. Cases due to Musca domestica[6] and Fannia fusconotata Rondani[7] have been recorded. The question arises as to how the organism enters the bladder. It may enter directly by passing up the urethra from swimming or bathing in contaminated water,[2] or it may migrate from the intestines.[1] DeGroot feels that gastrointestinal and genitourinary forms of the disease are very rare, but the genitourinary form may be caused by the laying of eggs about the urethra.[5]

There are numerous reported cases of gastrointestinal myiasis due to E. tenax.[8] Descriptions of E. tenax were published in 1909 by McCampbell and Corper and in 1912 by Hall and Muir.[4] That myiasis is often asymptomatic was shown by Kenney's work, in 1945, on feeding Leptocera venalicia to 60 men. Ten were completely asymptomatic, and the others noted few, if any, symptoms other than spontaneous passage.[9]

Summary

A case of genitourinary myiasis due to Eristalis tenax has been encountered. It is believed that no such case has been recorded previously. Gastrointestinal and genitourinary myiasis evidently is a

self-limited disease with spontaneous recovery after passage of the organisms as the usual outcome. There is no specific treatment.

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OPHTHALMOSCOPIC EXAMINATION IN CHILDREN

Jaime Quintanilla, M.D., Wilkes-Barre, Pa.

The purpose of this article is to present a simple technique which facilitates the ophthalmoscopic examination in children. During the neurological examination of the outpatients of the Children's Service Center of Wyoming Valley, Inc., the inspection of the optic fundi was not a simple procedure, because the children, particularly the very young ones, would keep their eyes in motion, attracted either by the light of ophthalmoscope or other objects in the examining room. Others would become frightened and would burst into tears and run to the door demanding to be taken to their parents.

We tried to solve the problem by asking the children to look at different pieces of equipment in the room, but the result was about the same. In one of these instances we decided to use a standard mirror, which produced the results here described. An 18-by-24-in. mirror was fixed on the wall 4 ft. from the floor. This location permitted a comfortable examination because the patient's face would be at about the level of that of the examiner. Very small children stood on a chair or were held by their parents.

The patients stood about 5 ft. from the mirror, except those under 3 years of age, who were held about 3 ft. from the mirror. With the room slightly illuminated, so as to allow the patient to see his face on the mirror, he was asked to look at his eyes. This fixed the eyeball, and the examiner proceeded. The children were helped with phrases such as "Keep looking at your eyes."

We found that, when the patient looked at the image of his eyes, the accommodation reflex entered into function, dilating the pupils which previously had been contracted by the stimulation from the light of the ophthalmoscope. Children found this experience interesting. Looking at what the examiner was doing not only immobilized their eyes but lessened the fear this examination often produced. It also "neutralized" the uncomfortable sensation of the light by concentrating their attention to the action seen in the mirror.

We have used this technique in over 75 patients from the age of 21 months and up. The results have been satisfactory in all but two cases; a severely mentally defective 5-year-old patient with hyperactive behavior was unable to cooperate, and a rather antagonistic youngster did not follow suggestions and resisted the entire neurological examination. In our series of patients we found only one abnormality, an early papilledema confirmed later by an ophthalmologist and found during a surgical exploration to be due to an acute arachnoiditis of the optochiasmatic area.

In conclusion, the dilatation produced by the accommodation reflex occurring when the patient looks at his image in the mirror was satisfactory for a routine inspection of the optic fundi. The combination of this effect with the immobilization of the eyeball and the cooperation of the patient makes this method a useful one.

335 S. Franklin St.

From the Children's Service Center of Wyoming Valley, Inc.

J.A.M.A., Aug. 9, 1958

MEDICAL CONTROL OF ADAMS-STOKES SYNDROME

Richard J. Jones, M.D., Chicago

Recurrent episodes of Adams-Stokes syncope due to ventricular arrest may occur in heart diseases of diverse etiology and pursue an unpredictable course. The clinical aspects of complete atrioventricular block and the Adams-Stokes syndrome have recently been reviewed,[1] and it has been well pointed out that the management of each case must be individualized.[2] Recently, the isopropyl derivative of arterenol, isoproterenol (Isuprel) hydrochloride, has been reported to exert a favorable influence on syncopal attacks due to complete atrioventricular block with a slow ventricular rate or to ventricular asystole[3] without increasing blood pressure substantially[4] or initiating or perpetuating ectopic ventricular arrhythmias.[3a] Most of the reported experiences with this agent have involved the use of oral linguets, though the use of continuous intravenous infusion has been employed by some workers[3b] and recommended by others.[2] The use of steroid therapy to enhance atrioventricular conduction has been suggested by the work of Lown and associates.[5] I have recently encountered a case of Adams-Stokes syndrome in which syncopal attacks, related to electrocardiographically established ventricular asystole, were occurring with mounting frequency and were favorably influenced by isoproterenol and, for a period of six months, by prednisone (Meticorten). After this period, an exacerbation occurred with frequent attacks which were no longer controlled by these medicaments, but symptomatic relief followed their withdrawal and the establishment of a permanent complete atrioventricular block.

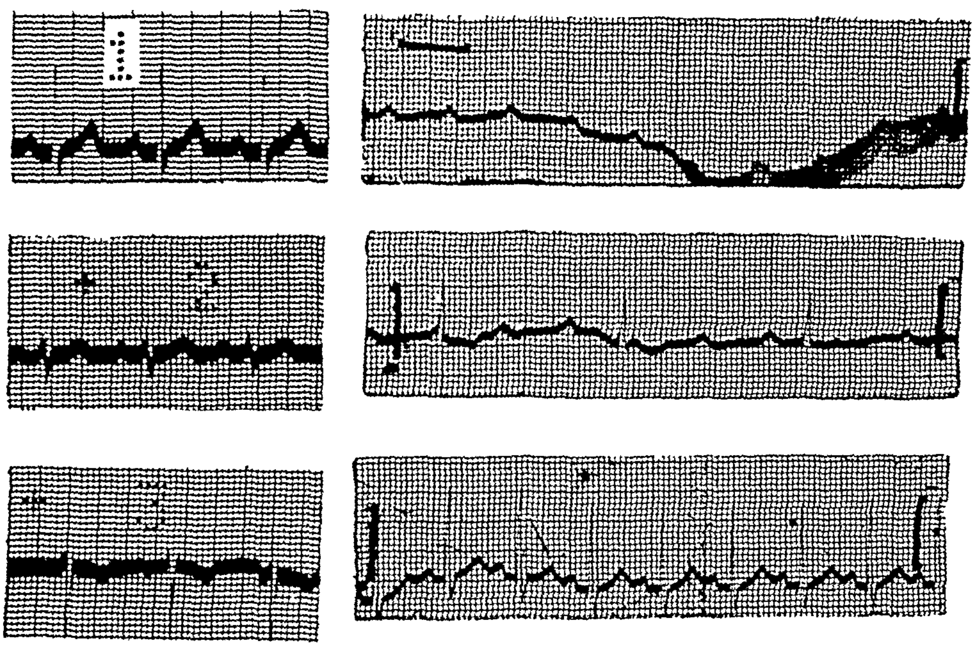

Fig. 1.—Electrocardiogram showing (*left*) standard limb leads on May 31, 1957, and (*right*) lead 1, taken during (*top*) ventricular arrest, (*middle*) complete atrioventricular block after the period of ventricular arrest, and (*bottom*) the restoration of a normal rhythm by intravenously given isoproterenol.

Report of a Case

A 40-year-old man was admitted to Billings Hospital on May 29, 1957, with the chief complaint of "black-out spells" of three months' duration. He had been in apparently excellent health until three months prior to admission, when he suddenly lost consciousness and fell to the floor one evening while sitting at the dinner table. One month later he had a second attack, identical in character, and this was then repeated with a progressive increase in frequency until he was having attacks three times a day by mid-April. At this time he was admitted to a local community hospital, where an electroencephalogram and an electrocardiogram were taken, and was treated with anticonvulsant drugs with apparent improvement. On his returning home, however, the incidence of these attacks increased again to several times a day so that he was readmitted to that hospital two weeks later. In spite of the fact that he was placed on anticonvulsant medication, the attacks increased in frequency so that he was having from 10 to 15 attacks of brief duration each day. Many times these occurred while he was asleep but more often while awake. They occurred at bed rest or in the upright position. Each attack was preceded by a burning sensation in both legs that rose into the chest and up into the head and lasted about five seconds before unconsciousness supervened. Unconsciousness never lasted more than two minutes, and convulsive movements had not been reported by any of numerous observers. At the time of admission to the neurology service of Billings Hospital, the patient was afraid to be left alone in a room for fear that he would hurt himself in falling.

The patient had undergone tonsillectomy in childhood and at the age of 28 had suffered a migratory polyarthritis, requiring five weeks of bed rest, diagnosed as acute rheumatic fever. To his knowledge, there had been no residual heart damage or any further rheumatic or cardiorespiratory symptoms.

The physical examination was not remarkable except that the heart, which was not seen to be enlarged, showed a grade-2 harsh systolic murmur at the apex, transmitting well toward the axilla. There was also a grade-2 systolic pulmonic murmur, lower in pitch and smoother in quality than that at the apex.

The initial electrocardiogram showed perfectly normal function, with a P-R interval of 0.20 seconds and left axis deviation (fig. 1, *left*). Findings on electroencephalogram, cisternal pneumoencephalogram, and manometric studies at the time of lumbar puncture were essentially negative. Routine determinations of hemoglobin level, white blood

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cell count, red blood cell count, hematocrit value, differential count, and sedimentation rate and urinalysis were negative. The antistreptolysin titer was 1:100, C-reactive protein precipitation 1+, and serum carbon dioxide content 28 mEq. per liter.

On the 18th hospital day, the patient had six spells in the first few hours of the morning and was seen by one of the house staff, who, for the first time, discovered that during an attack his pulse rate was 30-40 per minute and irregular. An electrocardiogram was then taken while the patient was under hyperventilation, and it was demonstrated that hyperventilation precipitated a complete atrioventricular block which was initiated by a period of ventricular asystole lasting up to nine seconds (fig. 1, *right*).

Treatment (see fig. 2).—With the establishment of this diagnosis, the anticonvulsant medication was discontinued and ephedrine, 30 mg. every three hours, sublingually given isoproterenol, 20 mg. every two hours, and hydroxyamphetamine (Paredrine) hydrobromide, 40 mg. every four hours, were tried without complete success. On the 23rd hospital day, the patient was started on therapy with 40 mg. of prednisone daily and intravenously given isoproterenol, 0.5 mg. per 100 cc. by a continuous intravenous drip. As long as the intravenous drip was maintained at a rate of 20 drops per minute (5 mcg. per minute), a normal sinus rhythm was maintained, usually at a rate between 90 and 110 beats per minute. The pulse rate fell slightly as the rate of infusion was decreased to 12 drops per minute, but at 12 drops or, sometimes, even 16 drops per minute the patient would develop an incomplete (2:1) atrioventricular block, which was productive of a vague uneasiness but not syncope. By the 27th hospital day, when the patient had been receiving 40 mg. of prednisone and about 30 mg. of intravenously given isoproterenol daily for four days, a slowing of the infusion rate to 10 drops per minute still permitted a lapse from a sinus rhythm to an incomplete atrioventricular block. On the 30th hospital day, after one week of therapy with isoproterenol administered intravenously, a normal sinus rhythm could be maintained with the isoproterenol infusion at 8 drops per minute, so that at this point the intravenous drip was replaced by sublingual therapy in the form of linguets of isoproterenol, 15 mg. every three hours. From this point on, there was no recurrence of any type of atrioventricular block or ventricular asystole until discharge from the hospital on the 50th hospital day.

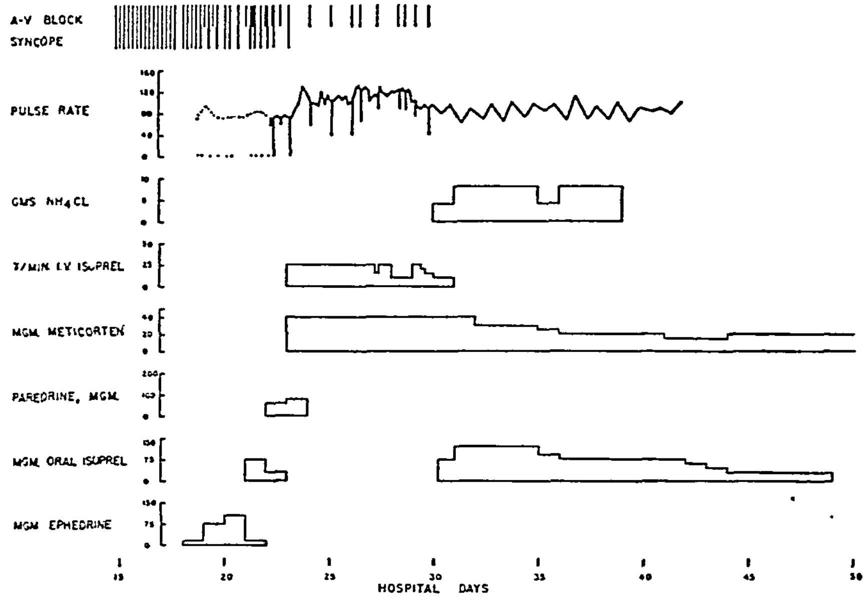

Fig. 2.—Observations on pulse rate and the presence of varying degrees of atrioventricular block with alterations in the treatment regimen during initial hospitalization.

The dosage of prednisone was gradually cut down over a six-week period, and the patient suffered no recurrence of symptoms until three weeks after the complete withdrawal of this drug, when attacks began to recur. He was then able largely to control the symptoms by returning to prednisone therapy, 15 mg. per day; syncopal attacks occurred rarely until this dosage was increased to 20 mg. per day. He took isoproterenol linguets only sporadically, because they provoked an "uneasiness," poorly described. On Feb. 1, 1958, approximately seven months after the initial admission, he began having a recurrence of "attacks" every 15 minutes, many of which were accompanied by loss of consciousness; these were not controlled by isoproterenol linguets or even by larger doses of prednisone. He was again hospitalized, and therapy with intravenously given isoproterenol was reinstituted. This time, even larger doses of the latter agent, ammonium chloride, and prednisone than were used before failed to maintain a constant sinus rhythm. Since it was again documented that his ventricular asystoles occurred only in the transition to complete block, it was decided that stabilization of the rhythm in a continuous atrioventricular block would be more desirable than keeping a tenuous sinus rhythm. To this end, prednisone and isoproterenol were withdrawn, and, when instability of the block became manifest by reversion to a sinus rhythm (usually at about the time of falling to sleep), therapy with neostigmine (Prostigmin), 15 mg. every three hours, was instituted. This fixed the block, which has remained stable with a ventricular rate of 36 to 40 per minute for over two months, except for a brief attack of gastroenteritis, of three days' duration, when a few syncopal attacks occurred.

Comment

The heart disease in the patient reported on above was of rheumatic etiology; hence, his conduction defect was most likely based on a rheumatic process in the region of the atrioventricular valve, though no laboratory tests suggested the presence of rheumatic activity and the original atrioventricular conduction time could not be considered abnormally prolonged. There was no historical or electrocardiographic evidence of coronary disease.

While it is obvious that a permanent cure was not effected, the intravenously given isoproterenol certainly carried the patient over a critical period when recurrent periods of asystole were threatening his brain and myocardium, if not his life. That prednisone therapy was the primary factor in ultimately controlling the conduction disturbance was not immediately clear, for he still developed incomplete atrioventricular block when the isoproterenol drip was slowed as late as the seventh day of prednisone therapy. In fact, the initial abatement of the Adams-Stokes syndrome may have had no relationship to the medication, for it is well known that such episodes can remit spontaneously for indefinite periods of time.[1]

Reports of occasionally successful treatment of cardiac arrest by thoracotomy and cardiac massage[6] or use of the external electrical pacemaker[7] suggest that these methods are helpful in surgical situations, where an acute and severe alteration in cardiac responsiveness may be reversible. It has been pointed out that these have no place in the type of case presented here[8]; a pharmacological approach is much more rational. As this case demonstrates, when a chronic process is depressing atrioventricular conduction, sympathomimetic and steroid agents may be used to their full capacity to strengthen it and, when this fails, parasympathomimetic agents may then be used to sustain the complete atrioventricular block, provided that a sufficiently rapid ventricular pacemaker can be maintained. Thus, control may be obtained over the great instability of the atrioventricular conduction, which is so conducive to ventricular asystole and the Adams-Stokes syndrome.

Summary

Successful control over recurrent episodes of cardiac arrest, heralding episodes of complete atrioventricular block, was obtained by continuous infusion of isoproterenol (Isuprel) hydrochloride in a patient for a period of one week. Return of a stable sinus rhythm was coincident with the supplemental use of ammonium chloride and prednisone (Meticorten), permitting withdrawal of the sympathomimetic agent for a period of six months. With return of the unstable rhythm, syncopal attacks were no longer prevented by these agents but were successfully avoided by stabilizing the complete atrioventricular block with neostigmine (Prostigmin).

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COMMITTEE ON MEDICOLEGAL PROBLEMS

THE PHYSIOLOGICAL ACTION OF ALCOHOL

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This report is chapter 2 from a manual, being prepared by the Committee of Medicolegal Problems, dealing with medical and legal procedures involved in the use of chemical tests for intoxication.

It is practically axiomatic that the acute action of any pharmacologically active substance is determined largely by the concentration in which it reaches its site of action. Thus in considering the effects of alcohol upon the human body, these can be better understood if we have some basic knowledge of the behavior of ingested alcohol in the physiological processes of the body—its absorption, distribution, and elimination.[1]

Absorption

Alcohol is absorbed through all mucous surfaces of the body. With ingested alcohol, absorption occurs in the upper portion of the gastrointestinal tract. Its comparatively small molecular size (as compared with other food stuffs) permits it to pass readily through membranes by simple diffusion, and, to a large extent, its absorption follows the principles of diffusion. The greater the difference in alcohol concentration in the fluids on two sides

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of a membrane, the more rapid is the diffusion rate from the side of higher concentration to the lower side.

Alcohol absorption may result from the injection of its solution into the body or by use of an alcohol-containing enema or douche or by inhalation of its vapors. In some instances motorists charged with driving while under the influence of alcoholic liquor have alleged that the alcohol in their body and on their breath resulted from the inhalation of alcohol fumes from an overheated automobile radiator. The absurdity of such claims was demonstrated by Lester and Greenberg.[2] These workers showed that inhalation of the highest tolerable concentrations of alcohol vapor produced only a minor elevation of the level of alcohol concentration in the blood. But since we are here concerned primarily with the effects of the alcoholic beverages, absorption from the gastrointestinal tract is of major interest.

When alcoholic liquor is swallowed, it is absorbed into the capillary circulation. Arterial blood is slightly higher in alcohol concentration than is venous blood, especially during the period of active absorption. The disparity between the two is not very great. Absorption takes place at a rapid rate, depending, among other things, on the quantity of alcohol ingested, its concentration in the drink, the nature and quantity of the diluting material already in the stomach, and the duration of its sojourn in the stomach.

When taken on an empty stomach, the alcohol from a single drink of liquor has been about 90% absorbed by the end of the first hour. It appears that absorption from the upper portion of the small intestine is even more rapid than the penetration through the stomach wall. It is generally observed that, following massive gastrectomy, patients complain that they become highly sensitive to alcoholic liquor and become noticeably intoxicated by doses which would have been quite innocuous prior to the operation. The speed with which stomach contents pass from the slowly absorbing surfaces of the stomach to the rapidly absorbing small intestine undoubtedly plays an important role in determining the rate of alcohol absorption.

It is well known that alcoholic liquor consumed after a meal has less intoxicating effect than the same amount of liquor taken on an empty stomach.[3] This has been shown to result from the slowing of alcohol absorption by the material in the stomach. This slowing is due, not simply to dilution by the large volume of stomach contents or the slowing of their passage into the rapidly absorbing small intestine, but also to the coating of the stomach by less permeable food components. It has been known that certain fatty foods such as milk, cream, or olive oil could inhibit alcohol absorption, but many nonfat food stuffs do just about as well. Tuovinen[4] found that a good-sized helping of mashed potatoes was one of the best deterrents of alcohol absorption. Habituation to the use of alcoholic liquors does not materially alter the rate of alcohol absorption; chronic alcoholics appear to absorb alcohol from the gastrointestinal tract at least as rapidly as do abstainers.[5] At high altitudes alcohol is absorbed more rapidly and produces higher blood alcohol concentrations than at sea level.[6]

Distribution

As soon as alcohol enters the blood stream it penetrates into the water of other tissues as well. When equilibrium has been reached (within an hour after drinking), alcohol will be found in all tissues of the body in proportion to their water content. Thus portions of the body which are richest in water content (urine, blood plasma, saliva, brain, liver, or kidney) will have the highest concentration of alcohol, whereas those of low water content (large bones or fat) will have the lowest alcohol concentration. After alcohol equilibrium has been reached, one may, with reasonable accuracy, estimate the alcohol content of any particular body material if one knows the alcohol concentration of any other portion of the body. Thus if one knows the alcohol content of the whole blood (which has become the common "yardstick" for expressing the alcohol content of body material) one may calculate the concentration of any other body material. The following ratios are typical: ureteral urine, 1.2 to 1.4 (depending upon specific gravity of urine[7]); blood plasma or serum, 1.10 to 1.15; cisternal spinal fluid, 1.10; saliva, 1.10 to 1.20; whole blood, 1.00; brain or liver, 0.85 to 0.90; kidney, 0.83; and alveolar breath, 1/2,100. (One volume of blood will contain the same amount of alcohol as will 2,100 volumes of alveolar [deep lung] breath.)

The rate at which alcohol equilibrium is reached in its distribution via the blood stream varies somewhat with different individuals and under differing circumstances. If drinking is at a slow steady rate, alcohol distribution to the tissues follows along at the same pace as absorption. However, if a person drinks a large volume of strong alcoholic liquor in a short time, on an empty stomach, alcohol distribution to the tissues lags behind the rapid absorption of alcohol into the blood stream.

Elimination

Following its absorption, alcohol is rapidly eliminated from the body, chiefly by oxidation to carbon dioxide and water. This oxidative metabolism ac-

COUNCIL ON MEDICAL SERVICE

NATIONAL HEALTH SURVEY

The 84th Congress authorized the U. S. Public Health Service to conduct a continuing study of the extent of illness and disability in the population of the United States and related information. For some months, the Department of Health, Education, and Welfare has been publishing periodic reports of the incidence of respiratory diseases gathered by this National Health Survey; now it has issued the first of its over-all studies on health and health care in the United States.[1]

Gathered by interviewers from some 9,000 households, comprising 28,500 persons, this preliminary report gives data on the frequency of physician visits, distribution of visits by place and by type of service, and the time interval between physician visits. Physician visits, for the purposes of the study, mean consultation with either doctors of medicine or osteopaths, in person or by telephone, for diagnosis, treatment, or advice. Mass services (e. g., mass chest x-ray services) and inpatient visits to hospitalized persons are excluded. Interviewers limited their questions to the two-week period before the interview, in order to avoid forgetfulness or distortion of health histories.

Over the 13-week quarter covered in the preliminary report, extension of the data indicates that there were about 199 million physician visits made in the United States, an annual rate of 4.8 visits per person.

The preliminary report indicates that this continuing study may provide intriguing and possibly helpful light on several medical problems. For example, the type of residence of the patient appears to have a definite effect on the pattern of medical practice: farm residents averaged 3.6 visits per year, compared with 4.5 visits for those in rural nonfarm residences and 5.1 for urban residents. Farm residents are more likely to visit the physician's office than are urban residents; 9% of the urban residents were visited at home, compared with only 4% of farm residents.

The location of the visit is also, apparently, affected by the age of the patient. On the average, 8% of all physician visits are in the home—but this average is brought up mainly by the young and the old patients. In the age group 15-44, only 4% of physician visits are home calls; for those 14 and younger, the percentage rises to 6%, for those 45-64, it rises to 10%, and for those 65 or older, to 21%.

Hospital clinic treatment averages 13% of all visits and appears to follow no set pattern of variation for patients under 65. However, the percentage drops abruptly from the 13% reported for patients 45-64 years of age to 7% for patients 65 and over. This older group is also slightly below the average for number of office visits.

Over two-thirds of all visits are for diagnosis and treatment, including visits for diagnosis or treatment only and diagnostic and therapeutic x-rays. About a tenth of the visits are for general checkups, including those for specific purposes, such as employment or insurance. Seven per cent are for immunizations and 4% for prenatal and postnatal care.

Immunizations are most frequent among the young, comprising 20% of the visits to children under 5 and 13% of those to children 5-14 years old. The percentage descends to 7% or 6% in the 15-44 age group and 2-1% in the 45-and-over group. General check-ups are also at the highest level (13%) in the under-5 group. The percentage drops to 11 to 12% for the 5-24 age group and to 8% for the 25-44 group but then begins to rise again, to 10 to 11% for those 45 and over. Visits for diagnosis and treatment remain below the 69% average up to the age of 45; in the 45-64 group they jump to 80%, with a slight drop to 78% for those 65 and over.

The trends for immunizations and diagnosis and treatment are readily understandable, since most immunizations are for childhood diseases and the frequency of disease increases with age. However, the pattern for general checkups may also be significant, as indicating patients are more likely to receive this service when under parental authority or when concerned about approaching old age than while in the middle years.

Apparently, the residence of the patient may also have some effect on the type of physician visit he emphasizes. Urban residents have approximately the average percentage of diagnostic and treatment visits, but rural farm residents are above average and rural nonfarm residents below; on the other hand, rural nonfarm residents are above average in immunization visits, while rural farm residents are below. Farm residents have less than half the percentage of prenatal and postnatal care visits for nonfarm residents.

Perhaps the most interesting feature of the report, however, is the data it provides on the differing pattern of medical care for men and women. The average woman had almost one and one-half times as many physician visits as the average man, 5.5 per year as against 3.9. In the two youngest age groups, there are more physician visits to boys than to girls—5 visits to boys under 5 against 4.6

to girls, and 3.6 to boys aged 5-14 against 3.2 to girls. However, in all other age groups visits to women are significantly more frequent than to men. Even in the older age groups, where maternity care becomes a minimal factor, the ratio remains high: 5.8 visits to women and 3.8 to men in the 45-64 age group, and 7.6 to women and 5.8 to men 65 and over.

Children under 14 have a comparatively equal number of visits regardless of sex, but visits to male patients drop from 3.6 per year in the 5-14 age group to 3.4 per year in the 15-24 group, increasing only slightly (to 3.8) in the 45-64 group. The frequency of visits to women, however, jumps from 3.2 in the 5-14 group to 6.3 in the 15-24 group, gradually decreasing to 5.8 in the 45-54 group. The big increase in visits for men does not occur until the over-65 group, when the average jumps to 5.8; *visits to women in this age group increase* by almost the same amount, to 7.6 per year.

The location of the visit also varies somewhat by sex. Both male and female patients have about 69% of their visits at the doctor's office, but, where men have about 7.6% of their visits at home and 15.2% at hospital clinics, women have almost 9.1% at home and only 10.8% at clinics.

The difference becomes more pronounced at advanced ages. Men over 65 actually make more office visits than the average—72.9% of all physician visits in this age group; their home visits rise to 11.4%, and clinic visits drop to 7.3%. The women in this age group, on the other hand, now have only 58.1% of their visits at the doctor's office, and clinic visits drop to about 7.4%—but home visits rise to 27% of the total.

The report notes that maternity care may be a factor in the higher rate of visits for women, but, even eliminating prenatal and postnatal care, physician visits for women still average 5.1 per year, as against 3.9 per year for men. Women had 3.7 visits for diagnosis and treatment, while men had only 2.8, and women averaged a slightly higher number of visits for general checkups, immunizations, and other procedures.

In the patients under 14, girls averaged a slightly higher number of physician visits for diagnosis and treatment and slightly lower for general checkups and immunizations than did boys. In the 15-24 age group, women averaged as many physician visits for diagnosis and treatment as men did for all purposes and also averaged more visits for checkups and immunizations.

In the 25-44 age group, women averaged more diagnostic and treatment visits than did men for all purposes; they still averaged more checkups but only the same number of immunization visits as men. In the 45-64 age group, the average woman made one and one-half times as many diagnostic and treatment visits as the average man, slightly more checkup visits, and three times as many immunization visits.

After 65, the gap shortens somewhat. Women in that age group had only one and one-third as many diagnostic and treatment visits, on the average, and both sexes averaged the same number of checkups. However, a small number of women's visits were still devoted to immunizations, while this purpose dropped out for men over 65.

Women in the 15-24 group averaged 1.4 visits for maternity care, and those in the 25-44 group averaged 0.7 visits; even omitting this care, in these age groups women averaged one and one-half to two times the total number of physician visits to men.

The report notes that three out of five persons had consulted a physician within the preceding year and one out of five within the preceding month. Only 9% had not consulted a physician within the past five years. At all ages from the 15-19 group on, a larger percentage of women than of men had seen a physician during the year.

Obviously, the survey is only in its initial stages, and data are insufficient for any firm conclusions. However, if preliminary figures are borne out in later studies, it is apparent that this greater number of physician visits, especially during youth and middle age, will bear further consideration as a factor in the greater longevity of women.

Summary

The preliminary report on physician visits from the National Health Survey indicates that the average person visits a physician 4.8 times per year and that most of the visits are for diagnosis and treatment. The rural resident, and especially the farm resident, visits the physician less frequently than the city-dweller and is more likely to go to the physician's office. Home calls are more frequent for the city-dweller, for young children, and, especially, for persons over 65.

The average man spends more visits on immunizations and checkups as a child than the average woman but then makes less physician visits after the age of 15 and does not greatly increase the frequency of visits until he is 65 or over. Women make more diagnostic and treatment visits at all ages and more over-all physician visits than men from the age of 15 on, doubling rather than decreasing the number of visits at the age of 15. The average woman is more likely to be visited at home and less likely at a clinic than a man; after 65, men make more visits to physicians' offices, while women make fewer such visits, receiving over a quarter of such care at home.

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MEDICAL NEWS

CALIFORNIA

Student Grants for Summer Fellowships.—Twenty-four students in the University of Southern California School of Medicine, Los Angeles, have received $16,000 in research and training fellowships for summer laboratory work supervised by members of the faculty. The individual grants range from $500 to $1,000 each. Donors were: Gamma Beta Chapter of Pasadena of Delta Theta Tau, national philanthropic sorority; National Foundation for Infantile Paralysis; Tobacco Industry Research Committee; Lederle Laboratories; U. S. Public Health Service; National Science Foundation; American Cancer Society; and Allergy Foundation of America.

Dr. Loosli Comes to Los Angeles.—The new dean of the University of Southern California School of Medicine, Los Angeles, Dr. Clayton G. Loosli, took office July 1. Dr. Loosli came from the University of Chicago, where he has been since 1938, the past nine years as professor of medicine and chief of the section of preventive medicine. Dr. Loosli, welcomed by the faculty at a reception June 30, was guest at a dinner given by the University of Southern California's vice-presidents and eight doctors who have run the School of Medicine the past two years since the resignation of Dr. Gordon E. Goodhart, who returned to private practice. Dr. Loosli is a member of the committee on environmental hygiene and an associate member of the committee on influenza of the Armed Forces Epidemiological Board. He is a fellow of the American College of Physicians and is a past-president (1955) of the Central Society of Clinical Research.

KANSAS

Dr. Greaves Named Head of Department of Psychiatry.—Dr. Donald C. Greaves has been named professor of psychiatry and chairman of that department in the University of Kansas School of Medicine, Kansas City, effective July 1. Dr. Greaves, who has been associate professor at the University of Oklahoma School of Medicine, Oklahoma City, since 1955, was instructor in psychiatry at the Cornell University Medical College, New York City, 1951-1954. He completed certification requirements of the American Board of Psychiatry and Neurology in 1956 and is a fellow of the American Psychiatric Association. Dr. William F. Roth Jr., who has been chairman of the department of psychiatry at the school since 1946, remains as full professor at the Kansas University Medical Center. He will devote more time to research and teaching.

LOUISIANA

Study of Cardiovascular Lesions in Baboons.—A study of cardiovascular lesions of baboons in their native environment has been launched by a team from the Louisiana State University School of Medicine, New Orleans. Arriving in Nairobi, Kenya Colony, Africa, in July, were Dr. Henry C. McGill Jr. and Dr. Jack P. Strong, of the department of pathology, and Joseph H. Miller, Ph.D., department of microbiology. Mr. Nicholas Gagliano, pathology instructor and museum curator, preceded them to set up equipment for the project. The research, financed by a grant from the Louisiana Heart Association, will be supervised by Dr. Russell L. Holman, head, department of pathology. The investigators, with assistance of persons in Kenya, will autopsy 300 baboons for these studies, and the information collected will be used as control data for future experiments to be conducted in the United States on live animals.

Dr. Fox Named Director of Public Health Division.—Dr. John P. Fox, professor of epidemiology, Tulane School of Medicine, New Orleans, has been appointed director of the Division of Graduate Public Health at Tulane. In this capacity he will become the administrator of Tulane's graduate training program in public health and tropical medicine. Dr. Fox has also been designated to become the first occupant of The William Hamilton Watkins chair in epidemiology established by Mr. and Mrs. Charles E. Inbusch, of Milwaukee. Tulane's degree-granting program in public health and tropical medicine, established in 1947, is one of 12 in North America. From 1938 through 1949, Dr. Fox was a staff member of the International Health Division of the Rockefeller Foundation, working chiefly in yellow fever and typhus. In 1949 he joined the faculty of the department of tropical medicine and public health at Tulane as professor and head of the division of epidemiology.

MARYLAND

Medical Licensure for Graduates of Foreign Medical Schools.—All graduates of foreign medical schools may be accepted for medical licensure in

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Maryland after completion of three years training in approved American hospitals, one year of which must be a rotating internship or one year of residency in internal medicine; and, also, one of the three years must be served in an approved hospital in the State of Maryland, if their credentials have been approved and they have presented at least two letters from medical authorities in the hospitals recommending them as to their professional ability and moral character. Licensure is on the basis of examination only. A Certificate of Naturalization or formal Declaration of Intention for citizenship is required. Ability to write and speak English clearly is a primary requisite. A passing grade of 75% in each subject is required of all candidates. Effective Jan. 1, 1959, all graduates of foreign medical schools must first take and pass the Screening Board Examination given by the Educational Council for Foreign Medical Graduates before being eligible to take the Maryland State Board examination.

MASSACHUSETTS

Appoint Chairman of Department of Urology.—Dr. George Austen Jr., of Cleveland, has been appointed professor of urology and chairman of the department at Boston University School of Medicine. Dr. Austen has been associate urologist at the University Hospitals, consultant in urology at the Crile Veterans Hospital, and assistant professor and assistant clinical professor of urology at Western Reserve University Medical School, all in Cleveland. Dr. Austen, who took special training in urology at Peter Bent Brigham Hospital, Boston, received the Harvey Cushing Fellowship and the George Gorham Peters Travelling Fellowship at the Harvard Medical School. He is a fellow of the American College of Surgeons and a diplomate of the American Board of Urology.

Dr. Brown Wins Medical Essay Contest.—Dr. Ethan A. Brown of Boston, editor, *Annals of Allergy*, is the winner of the 1958 Mississippi Valley Medical Society Essay Contest for his paper, "A Program for the Treatment of Subacute Bronchial Asthma." Dr. Brown, who will present his paper at the annual meeting of the Mississippi Valley Medical Society at the Hotel Morrison, Chicago, Sept. 24-26, will receive a gold medal, a certificate and a cash award of the society banquet, Sept. 28. The runner-up in the contest was Dr. Joseph Krimsky, of Huntington, W. Va., for his paper, "A Doctor's Credo," and third place went to Dr. Thorne J. Butler, of Chicago, for his paper, "Medicine's Role in the Population Problem." These papers will appear in the January issue of the *Mississippi Valley Medical Journal*.

MICHIGAN

Serum Albumin to Replace Liquid Blood Plasma.—The Michigan Department of Health has announced that henceforth it will supply only one human blood derivative—serum albumin—to physicians for treatment of shock. The department no longer will distribute liquid blood plasma, which it has supplied for shock treatment since 1942. Dr. Albert E. Heustis, state health commissioner, said that volume for volume, albumin is five times more effective than plasma in treating shock. Serum albumin is processed by the state health department from outdated whole blood from blood banks and from the blood contained in placentas contributed by Michigan hospitals participating in the department's blood salvage program. Dr. Heustis said that the state health department is remodeling its facilities for manufacturing serum albumin. Like other products manufactured by the state health department laboratories for the prevention or treatment of disease and illness among Michigan residents, serum albumin is distributed without charge.

MISSISSIPPI

Dr. Underwood Honored.—On his retirement as state health officer Dr. Felix J. Underwood, who became Mississippi's first full-time state health officer in 1924, was honored with a testimonial dinner in Jackson. Dr. Underwood directed the organization of local health departments in the 74 counties that were without full-time health protection, which incorporated sanitation programs, immunization programs, and case-finding activities in tuberculosis, venereal disease, and hookworm. His successor will be Dr. Archie L. Gray.

MISSOURI

State Medical Election.—The following officers of the Missouri State Medical Association have been installed: president, Dr. Wenceslaus F. Francka, Hannibal; president-elect, Dr. Ralph Perry, Kansas City; vice-presidents, Drs. James C. Cope, Columbia, Milton T. English Jr., Kirksville, and William O. Finney, Chaffee; treasurer, Dr. Raymond O. Muether, St. Louis; secretary, Dr. John I. Matthews, Jefferson City; editor, Dr. Charles R. Doyle, St. Louis; speaker of the house of delegates, Dr. Oscar P. Hampton Jr., University City; vice-speaker, Dr. William C. Mixson, Kansas City.

Personal.—Edward A. Doisy Sr., Ph.D., Nobel pirze winner and director of the Edward A. Doisy Department of Biochemistry, Saint Louis University School of Medicine, received an alumni achievement award at commencement exercises held at the University of Illinois, Urbana, June 14. In 1943 Dr. Doisy shared the Nobel Prize in Medicine with

Prof. Henrik Dam for isolating and determining the constitution and synthesis of vitamin K.—Dr. Grayson L. Carroll, associate professor of clinical urology, Saint Louis University School of Medicine, represented the American Urological Association in a study of urology and other medical work conducted in Russia when he spent 11 days in Moscow and Leningrad during the month of July.—Dr. Carl V. Moore, chairman, Board of Medicine, Washington University School of Medicine, St. Louis, has been appointed to serve through September, 1962, on the National Advisory Arthritis and Metabolic Diseases Council.

Fall Clinical Conference in Kansas City.—The annual Fall Clinical Conference of the Kansas City Southwest Clinical Society will be held Sept. 22-25 at the Municipal Auditorium. The sixth Edward Holman Skinner Memorial Lecture, "The Mechanism of Abdominal Pain," will be presented by Dr. Henry L. Bockus, Philadelphia. Other guest speakers include: Capt. Norman Lee Barr, M. C., U. S. Navy, Washington, D. C.; and Drs. Joseph H. Boyes, Los Angeles; Richard B. Capps, Chicago; Irving S. Cooper, John A. Evans, and George T. Pack, New York City; C. Rollins Hanlon, St. Louis; Jerome S. Harris, Durham, N. C.; John C. Harvey, Baltimore; Garth L. Jarvis, Galveston, Texas; Robert P. McCombs, Boston; Raymond D. Pruitt, Rochester, Minn.; John R. Schenken, Omaha; and Harry M. Spence, Dallas. Twenty-five round-table luncheons Sept. 23, a quiz session Sept. 24, and a combined medical and surgical luncheon closing with a panel discussion, "Recent Advances in Medicine and Surgery," Sept. 25 are planned. Two-day to four-day postgraduate breadfast seminars will be held. The following will be presented as the colored television program: radioactive isotopes; new electronic aids in medical diagnosis; operative cholangiography; nonspecific suppurative disease of the lung. For information write Dr. William M. Kitchen, Director of Clinics, Kansas City Southwest Clinical Society, 3036 Gillham Road, Kansas City 8, Mo.

NEW YORK

New York City

Venezuelans Begin Training in Rehabilitation.—Three Venezuelans, the first of a group of 25, have arrived in New York to begin training in rehabilitation methods in the United States. The three trainees, Dr. Jorge Dao Dao, Dr. Gilbert Montenegro, and Miss Ursula Hahn, started their programs of study July 14 at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center. They are all from Caracas. The project is administered by the World Rehabilitation Fund, a voluntary agency, with a three-year grant from the Sinclair Oil Corporation, through its Venezuelan affiliate, the Sinclair Venezuela Oil Company.

Dedicate Medical Research Laboratories.—Dr. William Smith Tillett was honored June 24 in The Bellevue Hospital Center when new research laboratories of New York University College of Medicine's department of medicine were dedicated in his name. Dr. Tillett retired July 1 as professor and chairman of the department and as director of the third medical (NYU) division of the Bellevue Hospital Center. A bronze plaque in honor of the occasion, presented by Dr. Colin M. MacLeod reads in part: "These laboratories named in honor of William Smith Tillett . . . are a symbol of his guiding principle that research in the problems of disease is essential to good medical care of patients and proper instruction of students and physicians." About 15 rooms comprise the laboratories, built and equipped at a cost of $180,000 through funds from the U. S. Public Health Service and a Commonwealth Fund grant to New York University-Bellevue Medical Center.

NORTH CAROLINA

Center for Study of Aging.—The Duke University Regional Center for the Study of Aging was established in 1957 under provisions of a $1,500,000 grant from the U. S. Public Health Service to bring the resources of medicine, psychiatry, sociology, biology and other fields to bear on the problems of elderly persons. Dr. Ewald W. Busse, chairman of the Duke Medical School's psychiatry department is principal investigator for the center. One major effort of the center is directed toward investigating body changes during the later years of life. Another research team is studying "age awareness," or what makes a person feel older or younger than his actual years. Other projects are concerned with the influence of emotional states on various body processes in the aged; with the ways that a person's adjustment to the years after retirement is related to his educational background, religion, occupational status and income; with skin problems of elderly people such as itching and premalignant lesions; with the role of cholesterol in the body and its relationship to atherosclerosis; and with the part that physical slowing down plays in the social and psychological adjustment of the aging person. In North Carolina, more than 286,000 persons reportedly are 65 or older and this number is increasing by about 7,000 each year.

OKLAHOMA

Plan Hospital and Health Center.—Groundbreaking ceremonies were held in Chickasha April 13 for the new Grady County Hospital and Health Center. Total project cost will be $1,440,000, the funds for which were provided by a county bond issue and Hill-Burton federal aid. On the ground floor of the hospital will be an administrative section, service areas, adjunct facilities, and one 30-bed medical nursing unit. The second floor will have a 30-bed medical and surgical nursing unit, surgical suite, and obstetrical suite. The basement will house storage facilities, mechanical equipment, and laundry space. Air-conditioning will have individual room controls. In each patient's room, provisions will be made for television, telephone, audio nurse's call system, toilet room, and oxygen. Buildings are located on a seven-acre tract of land. The Health Center building is connected to the hospital by a covered walk. Completion of the construction is expected in April, 1959.

PENNSYLVANIA

Grant for Research in Virus Effects.—The University of Pittsburgh Graduate School of Public Health has received a $151,800 research grant to study the effects of animal viruses on human malignant tissues. The national cancer institute awarded the grant, which will cover a three-year period. Dr. William McD. Hammon, head of the department of epidemiology and microbiology, will direct the project. Seven staff members will be working full time on the project and health area personnel, particularly in the medical school's department of pathology, will be serving as consultants. Dr. Davis S. Yohn, research associate in Dr. Hammon's department, will serve as co-investigator on the project. Dr. Hammon's team recently completed 18 years of research sponsored by the National Foundation for Infantile Paralysis. This same research team will staff the new cancer project.

Society News.—The Pennsylvania Radiological Society has elected the following officers for the year 1958-1959: Drs. John H. Harris, Harrisburg, president; Paul C. Swenson, Philadelphia, president-elect; Lester M. J. Freedman, Pittsburgh, first vice-president; Richard R. Hoffman, Lebanon second vice-president; Walter P. Bitner, Harrisburg, secretary-treasurer; and Carl B. Lechner, Erie, editor. The next annual meeting will be held in Harrisburg, April 24-25, 1959.——The following officers of the Pennsylvania Academy of Physical Medicine and Rehabilitation have been elected: president, Dr. William J. Erdman II, Philadelphia; vice-president, Dr. Nathan Sussman, Harrisburg; secretary-treasurer, Dr. Joseph M. Johnston, Pittsburgh; and program chairman, Dr. Samuel Sherman, Pittsburgh.——The Society of Nuclear Medicine of Pittsburgh has elected the following officers for 1958: Dr. Eugene R. Kutz, president; Dr. Paul R. Ritter, vice-president; and Dr. Paul M. Meadows, Presbyterian Hospital, secretary-treasurer.

Philadelphia

Dr. Matthews Named Psychiatry Department Head.—Dr. Robert A. Matthews has been appointed head of the department of psychiatry, Jefferson Medical College, effective July 1. Dr. Matthews, who resigned from his post of state commissioner of mental health, has been serving as professor of psychiatry at Jefferson since Sept. 1, 1956. He succeeds Dr. Baldwin L. Keyes, who will continue as emeritus professor. Dr. Matthews came to Jefferson from the Louisiana State University School of Medicine, New Orleans, where he had been head of the department of psychiatry and neurology since 1950. Dr. Matthews was president of the Philadelphia Psychiatric Society in 1947.

Announce Awards for Medical Writing.—The Silberman prize for medical writing, awarded by the Delaware Valley Chapter of the American Medical Writers Association for the "best-written case histories" submitted by residents and interns in the Philadelphia area hospitals were awarded May 21. The first prize was given to Dr. Richard J. Golinko, resident at the Children's Hospital, for his case report of an infant who suffered from a pheochromocytoma. Honorable mention and cash prizes were also awarded to Drs. David C. Schechter (Jefferson Hospital), Albert L. Sheffer, II (Graduate Hospital, University of Pennsylvania) and Marvin A. Sackner (Philadelphia General Hospital). The board of judges included John Shaw, editor, *Pediatric Clinics of North America;* Steven Spencer, medical editor, *Saturday Evening Post;* Dr. A. Henry Clagett Jr., editor, *Delaware State Medical Journal;* and Dr. Hugh Robertson, chairman, publication committee, Philadelphia County Medical Society. This is the second annual award presented by the American Medical Writers Association in the Delaware Valley area.

TENNESSEE

Plan Research Center at Gailor.—The Tennessee Department of Mental Health and the University of Tennessee will join in the operation of a research center in Gailor Hospital. Laboratories in the basement of Gailor will be expanded for the center, where basic and clinical research will be done in some phases of abnormal chemical conditions associated with mental illness. Research will deal particularly with schizophrenia, but also will be done in other conditions where distrubances in body chemistry are suspected to contribute to disorders, such as in alcoholism. Dr. Theron S. Hill, chief of the department of psychiatry, will be in charge of the research program. He is also psychiatric consultant for the Alcoholic Rehabilitation Center, and the research program will study disturbances of chemistry in patients in the rehabilitation center. Equipment will be provided by the State Mental Health Department. Dr. Cyril J.

Ruelmann, state comissioner of mental health, said the state would spend $50,000 to set up the center and about $10,000 per year to operate it. The university will share in the expense of the operation.

TEXAS

Foundation Plans Study of Discharged Mental Patients.—The Hogg Foundation for Mental Health of the University of Texas is planning a research project to study the problems of discharged or furloughed mental hospital patients as they attempt to readjust to community living. The director and co-directors of the project are Robert L. Sutherland, Ph.D., and Wayne H. Holtzman, Ph.D., of the foundation and Dr. Robert C. Rowell, superintendent of the Terrell State Hospital. Fred R. Crawford, Ph.D., a sociologist formerly dean of student life at Trinity University, San Antonio, has been appointed field coordinator. The tentative medical advisory committee consists of Dr. Robert L. Stubblefield, chairman of the department of psychiatry, Southwestern Medical School of the University of Texas, Dallas; Dr. Warren S. Williams, of the department of neurology and psychiatry, University of Texas Medical Branch, Galveston; and Dr. Donald P. Morris, in the private practice of psychiatry in Dallas. In addition, help in the planning has been obtained from Dr. Rawley E. Chambers, director of State Mental Hospitals and Dr. Eaton W. Bennett, superintendent of the San Antonio State Hospital. This study will not be concerned with medical problems or the therapy of patients, but will be "an attempt to gain some understanding of the adjustment problems which the patient meets in attempting to bridge the gap between the mental hospital and the resumption of normal family and community living." Observations will be made over a two-year period of discharged or furloughed state hospital patients in four communities of less than 50,000 population. The observation team will be composed of a psychiatric social worker and a social scientist. The Committee on Mental Health of the Texas Medical Association has supported this project and has helped in planning.

WASHINGTON

Appoint Dr. Wagner to Cardiovascular Research Chair.—Dr. Bernard M. Wagner, assistant professor of pathology at the University of Pennsylvania Medical School, Philadelphia, has been named by the University of Washington board of regents as the first appointee to the new Robert L. King Chair of Cardiovascular Research endowed at the university by the Washington State Heart Association. Dr. Wagner will assume his duties Aug. 1. The heart association announced in February that it would make $15,000 per year available to the university to employ a research scientist interested in heart disease and to help support his work. The grant is on a permanent basis. The Robert L. King Chair, the first endowed chair established at the university, honors Dr. Robert L. King, of Seattle, a past-president of the Washington State and American Heart Associations. Dr. Wagner will be an assistant professor of pathology.

HAWAII

Health Survey on Oahu.—The Oahu Health Survey will get underway in October with interviewers scheduled to call on 3,000 households. Plans call for the survey to be completed within a year. Questions will be asked on the prevalence of disease, injuries, and impairments; on the nature and duration of disability resulting from illness and injuries; and on the amount and type of medical care, dental care, and hospitalization utilized. Nine interviewers will be trained by Mrs. Katherine Capt, U. S. Census Bureau field worker. The survey is a cooperative venture of the USPHS, the Department of Health, and interested local agencies contributing funds for the survey. The Oahu Health Council is the coordinating agency. Final reports are expected early in 1960.

GENERAL

Conference on Cell Chemistry.—In celebration of the centenary of the publication of Rudolf Virchow's lectures on cellular pathology, a Conference on Chemical Organization of Cells Normal and Abnormal will be held Aug. 21-23 at Babcock Hall, the University of Wisconsin, Madison. Dr. John Z. Bowers will open the conference with an address. Twelve papers are scheduled to be presented at three sessions to include topics on cell development, nutrition, and structure, cell chemistry, and effects of enzymes, hormones, and viruses on cells. The meeting is sponsored by the Public Health Service, National Institutes of Health, Division of Research Grants. Registration fee is $10 and will include dinner and the reception Aug. 21. For information write Dr. Joseph F. A. McManus, University of Alabama Medical Center, 1919 Seventh Ave., South, Birmingham 3, Ala.

Meeting on Radiology in Denver.—The 20th Midsummer Radiological Conference of the Rocky Mountain Radiological Society will be held Aug. 14-16 at the Shirley-Savoy Hotel, Denver. Twenty papers are scheduled including two each by the following guest speakers: Drs. Ellwood W. Godfrey, Princeton, N. J.; Vincent P. Collins, Houston, Texas; John P. Caffey, New York City; Henry D. Diamond, New York City; and Leo H. Garland, San Francisco. Informal luncheon meetings, question-and-answer periods, and exhibits are planned. A panel on "Roentgen Film Diagnoses" will be held Aug. 16. A memorial lecturer in honor of Dr. James

P. Kerby, "A Review of the Clinical and Radiographic Features of Infantile Cortical Hyperostosis," will be presented by Dr. Caffey. At the informal banquet (Aug. 15), with Dr. Angus K. Wilson, president of the society, presiding, Dr. Garland will give "The Shadow of Research." For information write Dr. John H. Freed, 4200 E. Ninth Ave., Denver 20.

Society News.—The new officers of the American Association for Thoracic Surgery as elected in May are: president, Dr. Michael E. DeBakey, Houston, Texas; vice-president, Dr. William E. Adams, Chicago; treasurer, Dr. Julian Johnson, Philadelphia; secretary, Dr. Hiram T. Langston, Chicago; and editor, Dr. Emile F. Holman, San Francisco. After July 1 the official address of the secretary and headquarters office will be 7730 Carondelet Ave., St. Louis 5. The next meeting place will be Los Angeles April 21-23, 1959, with headquarters at the Hotel Statler.——At the 14th annual congress of The American College of Allergists, the following officers were elected to serve during 1958-1959: president, Dr. Merle W. Moore, Portland, Ore.; president-elect, Dr. Cecil M. Kohn, Kansas City, Mo.; first vice-president, Dr. Helen C. Hayden, Chicago; second vice-president, Dr. Philip M. Gottlieb, Philadelphia; and secretary, Dr. Maurice C. Harris, San Francisco. Dr. John D. Gillaspie, Denver, continues as treasurer.——The American Academy of Neurological Surgery has elected the following officers: president, Dr. Jess D. Herrmann, Oklahoma City; president-elect, Dr. Edwin B. Boldrey, San Francisco; vice-president, Dr. Samuel R. Snodgrass, Galveston, Texas; secretary-treasurer, Dr. Robert L. McLaurin, Cincinnati; historian, Dr. Howard A. Brown, San Francisco.

Invite Applications for Postdoctoral Fellowships.—Applications will be accepted through Sept. 2 by the National Science Foundation for a second group of postdoctoral fellowships to be awarded during 1958 in the regular postdoctoral program, Alan T. Waterman, foundation director, has announced. Fellowships will be awarded in the physical, medical, engineering, and other science fields, including anthropology, psychology (other than clinical), geography, certain interdisciplinary fields, and selected social science fields. Names of successful candidates will be announced Oct. 15. To be eligible, candidates must be citizens of the United States "with special aptitudes for advanced training" and must hold the doctoral degree or have the equivalent in training or experience. Fellows will be selected on the basis of ability as evidenced by letters of recommendation and other evidence of attainment. Final selection of fellows will be made by the National Science Foundation. A stipend of $3,800 per year will be awarded to successful applicants in the regular postdoctoral program. Dependency allowances will be made to married fellows. A limited allowance to aid in defraying a fellow's cost of travel will be paid as well as tuition and fees. Applications for the regular postdoctoral fellowships may be obtained by writing to the National Academy of Sciences–National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	July 12, 1958		July 13, 1957
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	2	2	2
Middle Atlantic States			
New York	..	..	4
New Jersey	3	4	1
Pennsylvania	..	..	..
East North Central States			
Ohio	..	..	8
Indiana	..	..	..
Illinois	..	2	7
Michigan	1	2	3
Wisconsin	..	..	7
West North Central States			
Minnesota	..	..	..
Iowa	..	..	2
Missouri	..	..	2
North Dakota	..	..	..
South Dakota	..	1	..
Nebraska	..	..	1
Kansas	..	..	..
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	..	1	7
West Virginia	5	7	1
North Carolina	1	2	7
South Carolina	1	1	6
Georgia	..	..	4
Florida	8	31	14
East South Central States			
Kentucky	..	..	5
Tennessee	2	3	7
Alabama	..	..	..
Mississippi	1	3	4
West South Central States			
Arkansas	..	..	3
Louisiana	2	2	2
Oklahoma	2	2	5
Texas	9	16	33
Mountain States			
Montana	..	12	..
Idaho	..	1	1
Wyoming	..	..	..
Colorado	..	..	..
New Mexico	..	2	3
Arizona	..	..	2
Utah	..	..	..
Nevada	..	..	1
Pacific States			
Washington	..	..	..
Oregon	1	1	1
California	6	9	25
Territories and Possessions			
Alaska	..	..	..
Hawaii	4	4	..
Puerto Rico	..	..	..
Total	48	108	183

CANADA

Canadian Medical Election.—The Canadian Medical Association has elected the following officers for 1958-1959: president, Dr. Arthur F. VanWart, Fredericton, N. B.; past-president, Dr. Morley A. R. Young, Lamont, Alta.; president-elect, H. R. H. The Duke of Edinburgh; deputy president-elect, Dr. Elmer K. Lyon, Leamington, Ontario; chairman of the general council and the executive committee, Dr. Norman H. Gosse, Halifax, N. S.; and honorary treasurer Dr. Gerald W. Halpenny, Montreal, P. Q.

CORRECTIONS

American Board of Radiology.—In the Examinations and Licensure section of The Journal, July 19, page 1536, the date for the regular examination for the American Board of Radiology is given as Dec. 8. The correct dates are Dec. 8-11, inclusive, and not Dec. 8 only.

Regulations for Reporting Blood Involvements.—Concerning a news item under this heading in The Journal, June 28, page 1129, Dr. Herman N. Bundesen, president, board of health, City of Chicago, has written that the correct wording of the first of the two regulations presented should read: "It shall be the duty of every physician, laboratory, and hospital to report immediately to the Chicago Board of Health by telephone Rh Negative mothers with a titre during a current pregnancy, and to confirm it in writing within 24 hours."

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application was June 23. Dates for the 1959 examinations have been set for Feb. 17 and Sept. 22. Executive Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

California: *Written Examination.* Los Angeles, August 18-21; Sacramento, Oct. 20-23. *Oral Examination.* Los Angeles, August 16; San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, June 15; Los Angeles, August 17; San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

Colorado: *Endorsement.* Denver, Oct. 14. *Written.* Denver, Dec. 9-10. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

District of Columbia:* *Reciprocity.* Washington, September 8. *Examination.* Washington, Dec. 8-9. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

New Hampshire: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

Montana: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 17-18. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

Ohio: *Examination.* Columbus, Dec. 16-18. *Endorsement.* Columbus, August 18; October 6 and Dec. 16-18. Sec., Dr. H. M. Platter, Wyandotte Bldg., Columbus 15.

Puerto Rico: *Examination.* San Juan, Sept. 2. Sec., Mr. Joaquin Mercado Cruz, Box 9156, Santurce.

South Dakota:* *Examination.* Rapid City, August 12-13. Exec. Sec., Mr. John C. Foster, 300 First National Bank Bldg., Sioux Falls.

Texas:* *Examination and Reciprocity.* Fort Worth, Dec. 4-6. Sec., Dr. M. H. Crabb, 1714 Medical Arts Building, Forth Worth 2.

Wisconsin: *Examination.* Madison, Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

Arkansas: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

Colorado: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

District of Columbia: *Reciprocity.* Washington, September 8. *Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Kansas: *Examination and Reciprocity.* Kansas City, Nov. 24-25. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Examination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

Oklahoma: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Texas: *Examination.* Oct. 13-14. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 19 and Milwaukee, Dec. 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

DEFENSE DEPARTMENT

Fellowship Training in Pathology.—The Armed Forces Institute of Pathology, Washington, D. C., now offers fellowship training of one year duration in the pathology of certain subspecialties of medicine and surgery to regular Army, Navy, and Air Force officers of the medical, dental or veterinary corps. Following are subspecialties in which fellowship training in pathology is offered: general surgery, dermatology, otorhinolaryngology, orthopedics, gynecology, neurology, urology, gastroenterology, cardiology, hematology, endocrinology, thoracic surgery, pediatrics, veterinary medicine, odontology, radiology, and ophthalmology. Officers selected for such training must have completed residency training and be either Board qualified or Board certified in the specialty in which training is sought. Applications should be submitted through the chain of command to the office of the surgeon general of the service concerned.

AIR FORCE

Consultants Visit Pacific Installation.—Drs. John Abajian of the University of Vermont College of Medicine, a consultant in anesthesiology, Louis J. West of the University of Oklahoma Medical Center, a consultant in psychiatry, and Gilbert H. Marquardt of Chicago, a consultant in internal medicine, recently visited Air Force medical installations in the Pacific to provide advice on problem cases and present lectures and teaching sessions.

Personal.—Major Gen. Dan C. Ogle, Air Force Surgeon General, received the honorary degree of Doctor of Laws, June 8, from his Alma Mater, Eureka College, Eureka, Ill. General Ogle also presented the commencement address.

VETERANS ADMINISTRATION

Personal.—Dr. Daniel H. Miller, manager of the VA Hospital at Muskogee, Okla., will be transferred as manager of the VA Hospital at Montgomery, Ala. Dr. Alexander W. Kruger, former manager of the VA Hospital, Brooklyn, N. Y., has resigned from the VA.

PUBLIC HEALTH SERVICE

Grant for Ophthalmologist Travel Expense.—The Public Health Service's National Institute of Neurological Diseases and Blindness has announced a grant of $25,000 to help defray travel expenses of 43 ophthalmologists and ophthalmological scientists who are delegates to the 18th International Congress of Ophthalmology in Brussels, Sept. 8-12. The grantees come from 27 universities, hospitals, and research centers in 16 states and the District of Columbia. The Congress will mark the centenary of international ophthalmology. The first international meeting was held in 1857 in Brussels. Among the topics to be discussed are senescence (aging) in ophthalmology and orthoptic treatment of strabismus (eye muscle incoordination). Symposiums will also be held on radioactive isotopes in ophthalmology, cataracts, electroretinography, and glaucoma. The International Association for Prevention of Blindness and the International Organization Against Trachoma will hold meetings in Brussels during the Congress. Requests for information should be sent to the Secretary-General of the Congress, Prof. Jules Francois, 15, Place de Smet de Naeyer, Ghent, Belgium.

Conference on Staphylococcic Disease.—A conference on staphylococcic disease will be held at the Communicable Disease Center of the Public Health Service in Atlanta, Ga., Sept. 15-17. The conference was recommended by the American Hospital Association and will be attended by representatives of 40 hospital, medical, and other professional organizations. Its main purpose is to identify control measures which can be established in hospitals and communities to deal with the mounting problem of infections caused by bacteria resistant to antibiotic drugs. The conference agenda will be developed by a special committee under the co-chairmanship of Dr. C. A. Smith, deputy chief, communicable Disease Center, and Dr. Frederick Wentworth, chief, Communicable Diseases Unit of the Ohio Department of Health.

Conference on Public Health Training.—Public health leaders and educators will take part in a national conference on public health training July 28-30 at the Department of Health, Education, and Welfare, Washington 25, D. C. The conference has been called by Surgeon General Burney to assist in reviewing all public health training needs and resources and the traineeship program authorized by Congress in 1956 which has helped to finance the graduate training of almost 1,000 public health workers. Dr. Berwyn F. Mattison, executive secretary of the American Public Health Association, will serve as chairman of the conference, and Dr. Malcolm H. Merrill, director of the California Department of Public Health, will act as secretary.

Personal.—On July 1, Dr. Paul Q. Peterson, a commissioned officer in the U. S. Public Health Service since 1942, became assistant director of the National Institute of Allergy and Infectious Diseases, Bethesda, Md. His previous experience includes service with the Ohio and Kentucky state health departments and a tour of duty in the Far East as chief of the Health Division of the Mutual Security Mission in China, Cambodia, Laos, and Vietnam.

DEATHS

Amster, Joseph Sidney, New York City; Long Island College Hospital, Brooklyn, 1911; member of the Medical Society of the State of New York; served as resident physician at the New York City Reformatory in New Hampton, N. Y.; died April 29, aged 72.

Baker, Frederick Edward ⊕ Detroit; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1925; on the staffs of the Mount Carmel Hospital and the Henry Ford Hospital, where he died June 4, aged 60.

Betthauser, Joseph R. ⊕ Hays, Kan.; Loyola University School of Medicine, Chicago, 1916; fellow of the American College of Surgeons; on the staffs of the Hadley Memorial and St. Anthony's hospitals; died June 4, aged 69, of myocardial infarction.

Brown, Frank E. ⊕ Salem, Ore.; Willamette University Medical Department, Salem, 1900; specialist certified by the American Board of Otolaryngology; member emeritus of the board of trustees at his alma mater; died June 8, aged 88, of cerebral thrombosis and arteriosclerotic heart disease.

Brown, John Edwin Jr. ⊕ Columbus, Ohio; born in Columbus May 25, 1903; Harvard Medical School, Boston, 1929; certified by the National Board of Medical Examiners; specialist certified by the American Board of Pediatrics; fellow of the American Academy of Pediatrics; president of the Central Ohio Pediatric Society in 1955-1956; chairman of the board of trustees and member of the council, Columbus Academy of Medicine; member of Phi Delta Theta, Phi Beta Kappa, Nu Sigma Nu, and Alpha Omega Alpha; veteran of World War II; since 1947 clinical associate professor of pediatrics at the Ohio State University College of Medicine; trustee of the Columbus School for Girls; associated with the Children's, Grant, Mount Carmel, Ohio State University, and White Cross hospitals, and the St. Ann's Hospital for Women; died suddenly June 3, aged 55, of a heart attack.

Bryer, James Allen Sr., North Attleboro, Mass.; Boston University School of Medicine, 1899; veteran of World War I; for many years on the staff of the Sturdy Memorial Hospital in Attleboro, where he died May 31, aged 84.

Burnett, Donald Richard, Denver; University of Colorado School of Medicine, Denver, 1954; an associate member of the American Medical Association; resident, University of Colorado Medical Center; drowned June 1, aged 28, when his canoe overturned in the Las Animas River.

Cahana, Stephen ⊕ Milwaukee; born in 1880; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; served as associate clinical professor of medicine emeritus at the Marquette University School of Medicine; past-president and for 28 years associated with the state board of health; at a testimonial dinner in Madison received a certificate of public service and was honored by Gov. Walter J. Kohler and members of the board of health and the State Medical Society of Wisconsin, which presented him with a silver plaque; served as chief physician of the city fire department; died in Los Angeles June 1, aged 76, of acute coronary occlusion.

Clark, John Aloysius ⊕ Gilroy, Calif.; Medical Department of the University of California, San Francisco, 1907; died March 6, aged 78, of diabetes mellitus.

Clawater, Earl William ⊕ Tyler, Texas; University of Texas School of Medicine, Galveston, 1915; at one time on the faculty of his alma mater; served as president of the Smith County Medical Society; veteran of World War I; formerly on the staff of John Sealy Hospital in Galveston; associated with the Mother Frances Hospital and the Medical Center Hospital, where he died May 27, aged 66, of cancer of the esophagus.

Compton, William J., Crawford, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1895; died in the Goodall-Witcher Hospital in Clifton June 8, aged 86, of congestive heart failure.

Curtis, Richard Carleton ⊕ Bonham, Texas; born Jan. 23, 1890; Medical Department of Emory University, Atlanta, 1915; service member of the American Medical Association; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; past-president of the Texas Radiological Society; past-president of the Navarro County Medical Society and vice-president of the Bell County Medical Society; veteran of World War I; a member of the board of education of Temple and for four years city commissioner of Corsicana; served on the staffs of the King's Daughters' Hospital in Temple and the Veterans Administration Hospital; died in the Veterans Administration Hospital in Houston May 28, aged 67, of infarction of the right cerebral hemisphere.

⊕ Indicates Member of the American Medical Association.

Dishmaker, Melvin Charles ✠ Milwaukee; Rush Medical College, Chicago, 1927; on the staff of St. Mary's Hospital; died June 3, aged 54, of cerebral hemorrhage, following an operation for a malignant brain tumor, and terminal pneumonia.

Dratler, Maurice, Brooklyn; Medizinische Fakultät der Universität, Vienna, Austria, 1933; died June 1, aged 53.

Duckett, Claude E. ✠ Lamar, Mo.; University Medical College of Kansas City, Mo., 1909; served as state representative; died June 2, aged 72, of pulmonary tuberculosis.

Dunham, Royal Wade ✠ Miami, Fla.; Loyola University School of Medicine, Chicago, 1916; member of the Illinois State Medical Society; formerly medical director of the Ottawa (Ill.) Tuberculosis Sanatorium; died June 15, aged 67, of bronchopneumonia.

Erbacher, Christine, Buffalo; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1936; died June 1, aged 67, of carcinomatosis.

Figur, Leon ✠ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1926; died June 14, aged 57.

Fitch, Edward Rufus, Ashland, Ky.; Kentucky School of Medicine, Louisville, 1901; member of the Kentucky State Medical Association; associated with the King's Daughters' Hospital, where he died June 3, aged 85, of arteriosclerosis.

Forst, John Adolph ✠ Albany, N. Y.; Long Island College Hospital, Brooklyn, 1914; served as chief of the bureau of health service, New York State Department of Education; died May 31, aged 67, of coronary heart disease.

Gabor, Marcell Emil ✠ Milwaukee; Univerzita Komenského Fakulta Lékarská Bratislava, Czechoslovakia, 1921; associated with St. Michael and Evangelical Deaconess hospitals and St. Joseph Hospital, where he died June 6, aged 63, of coronary thrombosis.

Gamburg, Leo ✠ Moline, Ill.; University of Illinois College of Medicine, Chicago, 1931; fellow of the American Psychiatric Association; specialist certified by the American Board of Psychiatry and Neurology; at one time appointed a physician for the Illinois Department of Public Welfare; past-president of the Mental Health Center of Rock Island County; served on the staff of the East Moline (Ill.) State Hospital; died June 5, aged 58, of myocardial infarction.

Gaspar, Louis Alfred Rodrigues Jr. ✠ Honolulu, Hawaii; Stanford University School of Medicine, San Francisco, 1930; certified by the National Board of Medical Examiners; member of the American Academy of General Practice; served as secretary of the Hawaii Territorial Medical Association; died in San Francisco April 7, aged 54, of coronary occlusion.

Glenn, Charles Foster ✠ Rutherfordton, N. C.; University of Louisville (Ky.) School of Medicine, 1914; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; formerly secretary-treasurer of the Rutherford County Medical Society; served in the regular Navy; on the staff of the Rutherford Hospital, where he died June 1, aged 70.

Guild, B. Thurber, Sands Point, N. Y.; born in 1885; the Hahnemann Medical College and Hospital, Chicago, 1908; consultant of the Council on Pharmacy and Chemistry of the American Medical Association; past-president of the Dorchester (Mass.) Medical Society; served as councilor of the Massachusetts Medical Society, of which he was a member; member of the Society for Investigative Dermatology and the Society for the Study of Asthma and Allied Conditions; while in Boston was an attending physician at Massachusetts General Hospital and an instructor at Harvard Medical School; in 1943 became president of Fairchild Brothers and Foster, a subsidiary of Winthrop Laboratories, pharmaceutical manufacturers; appointed a medical director of Winthrop in 1945, continuing in that capacity until his retirement in 1955; later served as a consultant to several drug and cosmetic firms; died in the North Shore Hospital, Manhasset, L. I., N. Y., June 15, aged 72, of carcinoma of the head of the pancreas.

Hanna, Henry Pierce, Birmingham, Ala.; Birmingham Medical College, 1912; died June 3, aged 68.

Harriman, Cora Elizabeth ✠ Natick, Mass.; Tufts College Medical School, Boston, 1902; died April 3, aged 82.

Henderson, Thomas Bain ✠ Mobile, Ala.; Medical College of South Carolina, Charleston, 1943; served as county coroner; on the staff of the Mobile Infirmary and Providence Hospital; died June 1, aged 47, of coronary occlusion.

Jaffe, Marvin Phillip, Cleveland Heights, Ohio; Ohio State University College of Medicine, Columbus, 1956; interned at the Kings County Center in Brooklyn; served a residency at Albert Merritt Billings Hospital in Chicago; aged 27; was killed when struck by a truck April 17.

Kennedy, David Dickey, Pittsburgh; University of Pittsburgh School of Medicine, 1908; an associate member of the American Medical Association; on the staff of the Allegheny General Hospital, where he died April 17, aged 78.

Klein, Hugo Oswald, Collingswood, N. J.; Christian-Albrechts-Universität Medizinische Fakultät, Kiel, Prussia, Germany, 1898; an associate member of the American Medical Association; member of the Medical Society of the State of New York; died in Our Lady of Lourdes Hospital in Camden, March 7, aged, 85, of pulmonary embolism and acute bronchitis.

Lane, Stuart Frederic ✠ Camarillo, Calif.; University of California School of Medicine, San Francisco, 1927; member of the American Psychiatric Association; veteran of World War II; assistant to clinical director, Camarillo State Hospital; died in St. John's Hospital, Oxnard, May 27, aged 61, of ruptured abdominal aneurysm and arteriosclerosis.

Larson, Henry Maxwell ✠ Morristown, N. J.; Columbia University College of Physicians and Surgeons, New York City, 1914; veteran of World War I; served on the staffs of the Memorial and All Souls hospitals; died in the Roosevelt Hospital, New York City, June 5, aged 69.

Lerner, Ralph, Brooklyn; New York Homeopathic Medical College and Hospital, New York City, 1921; died in the Columbia (S. C.) Hospital April 17, aged 65.

Liber, Benzion, New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1904; specialist certified by the American Board of Psychiatry and Neurology; an associate member of the American Medical Association; served on the faculty of the New York Polyclinic Medical School and Hospital; formerly associated with the New York State Psychiatric Institute; psychiatrist for the New York City Department of Welfare; author of many books; died June 6, aged 83.

McConagha, Arthur Blanchard ✠ Lafayette, Calif.; Starling-Ohio Medical College, Columbus, 1909; member of the Ohio State Medical Association; formerly practiced in Ashley, Worthington and Columbus, Ohio, where he was on the staffs of the White Cross and Mount Carmel hospitals; died May 15, aged 80, of a cerebral vascular accident.

McLeod, Hugh Carroll ✠ Hattiesburg, Miss.; Tulane University School of Medicine, New Orleans, 1919; member of the Southeastern Surgical Congress; fellow of the International College of Surgeons and the American College of Surgeons; in 1938 president of the South Mississippi Medical Society; staff physician for the Mississippi Southern College; on the staffs of the Forrest County General Hospital and the Methodist Hospital; division surgeon for the Illinois Central Railroad; died in the University Hospital, Jackson, May 14, aged 63.

McPherson, Vernon Laster, Dallas, Texas; University of Arkansas School of Medicine, Little Rock, 1913; member of the Texas Medical Association; past-president of the Choctaw (Okla.) County Medical Society; veteran of World War I; on the staff of Methodist Hospital; died May 16, aged 69, of carcinoma of the liver and of the prostate.

Magraw, James Finney, Perryville, Md.; University of Maryland School of Medicine, Baltimore, 1909; past-president of the Cecil County Medical Society; an associate member of the American Medical Association; for many years director and president of the National Bank of Perryville; died March 27, aged 72.

Martin, Douglas Dickinson ✠ Tampa, Fla.; University College of Medicine, Richmond, 1913; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; fellow of the American College of Physicians; served as president of the Hillsborough County Tuberculosis and Health Association and the Hillsborough County Medical Society; veteran of World Wars I and II; associated with Tampa Municipal Hospital and St. Joseph's Hospital, where he died May 24, aged 68, of acute myocardial infarction and coronary arteriosclerosis.

Metzger, Jeremiah, Tucson, Ariz.; Rush Medical College, Chicago, 1901; member of the American Clinical and Climatological Association; member of the House of Delegates of the American Medical Association in 1926; served as superintendent of the Arizona State Hospital; died in St. Mary's Hospital May 26, aged 81, of ruptured aortic aneurysm and arteriosclerosis.

Michel, Henry Middleton ✠ Augusta, Ga.; University of Georgia Medical Department, Augusta, 1896; clinical professor emeritus of orthopedic surgery at Medical College of Georgia; veteran of World War I; died May 25, aged 82, of gastrointestinal hemorrhage.

Milburn, Kennedy Abbott ✠ San Antonio, Texas; Baylor University College of Medicine, Dallas, 1930; served on the staffs of Baptist Memorial, Robert B. Green, and Santa Rosa hospitals; died in the New England Baptist Hospital, Boston, May 14, aged 53.

Miller, Benjamin Franklin, Whittier, Calif.; Rush Medical College, Chicago, 1897; fellow of the American College of Surgeons; died May 25, aged 83.

Mills, Earnest Prudden, Ogden, Utah; born in Hickory Grove, Mo., Aug. 8, 1871; Kansas City (Mo.) Homeopathic Medical College, 1896; at one time a member and past-president of the Kansas State Board of Health; served on the faculty of his alma mater; in 1919 commissioned an inspector for the American Red Cross in the U. S. Army and was stationed at Irkutch, Siberia; formerly practiced in Olathe, Kan., and served as coroner of Johnson County; past-president of the Weber County Medical Society; on the medical staff of St. Benedict's Hospital; charter member of the medical staff of Thomas D. Dee Memorial Hospital, where he died May 19, aged 86, of arteriosclerotic cardiovascular disease.

Mills, William Merrill ⊕ Topeka, Kan.; born in Topeka Feb. 23, 1883; Columbia University College of Physicians and Surgeons, New York City, 1907; clinical professor emeritus of surgery at the University of Kansas School of Medicine, Kansas City, Kan.; member of the founders group of the American Board of Surgery; member of the Western Surgical Association, which he served as treasurer and vice-president; fellow of the American College of Surgeons; past-president of the Kansas Medical Society; on the staff and member of the board of trustees of the Stormont Vail Hospital; on the staff of St. Francis Hospital; surgical consultant at the Winter Veterans Administration Hospital and the State Hospital, member of the board of governors of Menninger Foundation; member of the board of directors of Merchants National Bank; for eleven years editor of the *Journal of the Kansas Medical Society;* died May 26, aged 75, of acute coronary disease.

Mithoefer, William ⊕ Cincinnati; Medical College of Ohio, Cincinnati, 1897; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and the American Otological Society; fellow of the American College of Surgeons; past-president of the Cincinnati Academy of Medicine; a member of the staff of Christ Hospital, where he died May 26, aged 82, of acute hemorrhagic pancreatitis with embolism of the mesentery.

Montgomery, Daniel Cameron ⊕ Greenville, Miss.; born Jan. 6, 1885; Jefferson Medical College of Philadelphia, 1910; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; past-vice-president of the Mississippi State Medical Association; veteran of World War I; chairman of the board, First National Bank, of which he was formerly president; on the staffs of the General and King's Daughters' hospitals; died May 29, aged 73, of congestive heart disease.

Moore, Cary Walton Charles ⊕ Talladega, Ala.; Birmingham Medical College, 1913; member of the Southeastern Surgical Congress; on the staff of the Citizens' Hospital; died May 28, aged 70, of cerebral thrombosis and arteriosclerosis.

Mosher, George, Miami Beach, Fla.; Cornell University Medical College, New York City, 1908; died in Newark, N. J., March 5, aged 70, of carcinoma of the liver.

Mott, William Henry ⊕ Farmington, Iowa; Keokuk (Ia.) Medical College, College of Physicians and Surgeons, 1900; served as president of the Van Buren County Medical Society; veteran of World War I; for many years a member of the board of education, and city health officer; died in the Memorial Hospital, Keosauqua, May 12, aged 84.

Mowry, George Edward, Hayes, Va.; Temple University School of Medicine, Philadelphia, 1952; member of the American Academy of General Practice; on the staff of the Riverside Hospital in Newport News; died in the Medical College of Virginia Hospital in Richmond June 3, aged 35, of leukemia.

Mundell, Minuette Smith ⊕ Hutchinson, Kan.; University of Kansas School of Medicine, Kansas City, 1914; on the staff of St. Elizabeth Hospital and the Grace Hospital, where she died April 24, aged 81, of cerebral hemorrhage and hypertensive cardiovascular disease.

Newell, Frank Fordyce, Burlington, Wis.; Northwestern University Medical School, Chicago, 1900; on the staff of the Burlington Memorial Hospital; died May 26, aged 78, of a neoplasm and intestinal obstruction.

Nohe, Carl Clyde ⊕ Akron, Ohio; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; veteran of World War I; editor of the *Bulletin of the Summit County Medical Society;* died May 17, aged 66.

Oberkrom, L. W., Kansas City, Mo.; St. Louis College of Physicians and Surgeons, 1901; died June 5, aged 83, of acute myocardial infarction.

Oppenheimer, Bernard Sutro ⊕ New York City; born in New York City June 20, 1876; Columbia University College of Physicians and Surgeons, New York City, 1901; specialist certified by the American Board of Internal Medicine; served on the faculty of his alma mater; member of the Association of American Physicians and the American Society for Clinical Investigation; fellow of the American College of Physicians; director of the New York Tuberculosis and Health Association; veteran of World War I; in 1917 received the gold medal from the American Medical Association for electrocardiographic exhibit, illustrating pathological physiology of the cardiac mechanism; associated with Mount Vernon (N. Y.) Hospital, Mount Sinai and Montefiore hospitals; died June 10, aged 81.

Paddleford, George Edgar, Lodi, Calif.; University of Southern California College of Medicine, Los Angeles, 1904; died in Santa Barbara May 13, aged 83.

Paine, Ruffin Baker, Mandeville, La.: Medical Department of Tulane University of Louisiana, New Orleans, 1888; an associate member of the American Medical Association; died May 25, aged 92, of coronary thrombosis.

Payte, James Ira ⊕ Oklahoma City, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1930; member of the American Academy of General Practice; veteran of World War II; on the staffs of the Wesley and Polyclinic hospitals; died May 27, aged 61, of a heart attack.

Pearce, Samuel Bemis, Delray Beach, Fla.; University of Pittsburgh School of Medicine, 1912; veteran of World War I; practiced in Pittsburgh; died in the Good Samaritan Hospital, West Palm Beach, April 27, aged 69, of cerebral vascular hemorrhage and hypertension.

Pink, John James ⊕ Milwaukee; Rush Medical College, Chicago, 1921; on the staffs of the Milwaukee Hospital and the Columbia Hospital, where he died May 28, aged 62, of bronchogenic carcinoma of the right lung.

Post, John Asa ⊕ Buffalo; University of Buffalo School of Medicine, 1919; fellow of the American College of Surgeons; associated with the Emergency Hospital of the Sisters of Charity, St. Francis Hospital, and Millard Fillmore Hospital, where he died May 9, aged 62, of carcinoma of the stomach and liver.

Pustai, Joseph Nicholas ⊕ Northampton, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1952; interned at the Sacred Heart Hospital in Allentown; served in the South Pacific during World War II; found dead May 19, aged 34, of a gunshot wound.

Redman, William Masterson, Miami, Fla.; Tufts College Medical School, Boston, 1933; died April 23, aged 50, of pulmonary emphysema and acute pulmonary edema.

Reed, Claude Carvell, Sheffield, Mass.; College of Physicians and Surgeons, Boston, 1937; died May 30, aged 56, of coronary thrombosis.

Reed, Paul A. ⊕ Iowa City, Iowa; State University of Iowa College of Medicine, Iowa City, 1907; associated with the Mercy Hospital, where he died April 27, aged 83, of carcinoma of the prostate with metastases.

Rieg, Philip William, Lake Worth, Fla.; Toledo Medical College, 1913; practiced in Toledo, Ohio, where he was on the staff of the St. Luke's Hospital; died May 31, aged 71, of a heart attack.

Riekert, Joseph George, New York City; Cornell University Medical College, New York City, 1938; member of the Medical Society of the State of New York and the American Urological Association; specialist certified by the American Board of Urology; associated with the Manhattan Eye, Ear and Throat Hospital and the Lenox Hill Hospital, where he died April 28, aged 44, of leukemia.

Riggin, Howard Sanford ⊕ Seaford, Del.; New York Homeopathic Medical College and Flower Hospital, New York City, 1916; past-president of the Medical Society of Delaware; formerly practiced in New York City; died in the Nanticoke Memorial Hospital May 31, aged 76, of uremia.

Roberts, Jordan Lucas, Nashville, Ark.; College of Physicians and Surgeons, Little Rock, 1910; died May 27, aged 87.

Rossman, Walter Buskirk, Albany, N. Y.; Albany (N. Y.) Medical College, 1892; member of the Medical Society of the State of New York; died in the Albany Hospital May 22, aged 88.

Roth, Augustus Henry, Erie, Pa.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; an associate member of the American Medical Association; fellow of the American College of Surgeons; served on the faculty of his alma mater; division surgeon for the New York Central Railroad for many years; emeritus chief of staff, St. Vincent's Hospital, where he died May 26, aged 78, of arteriosclerotic cardiovascular renal disease.

Schaumberg, Max ⊕ Jackson Heights, N. Y.; Philipps-Universität Medizinische Fakultät, Marburg, Prussia, Germany, 1910; died May 18, aged 72, of coronary occlusion, arteriosclerosis, and diabetes mellitus.

Schrayer, Joseph, Evanston, Ill.; National Medical University, Chicago, 1907; Hahnemann Medical College and Hospital, Chicago, 1909; died March 21, aged 85.

Scott, Garland Dix ⊕ Sullivan, Ind.; Rush Medical College, Chicago, 1908; at one time on the faculty of Northwestern University Medical College in Chicago; veteran of World War I; in 1929 member of the House of Delegates of the American Medical Association; fellow of the American College of Surgeons; on the staff of the Mary Sherman Hospital, where he died May 22, aged 74, of a cerebrovascular accident and osteoporosis of the spine.

Shackleton, William Elsworth ⊕ Richland, Mich.; born in La Grange, Ind., Jan. 4, 1883; Northwestern University Medical School, Chicago, 1909; fellow of the American College of Surgeons; veteran of World War I; past-president and secretary of the Kalamazoo Academy of Medicine; formerly practiced in Chicago, where he was on the faculty of his alma mater, and member of the staff of the Wesley Memorial Hospital; at one time practiced in Kalamazoo, where he served on the staffs of the Bronson Methodist Hospital and the Borgess Hospital, where he died May 31, aged 75, of arteriosclerotic heart disease, and diabetes mellitus.

Sherman, Louis ⊕ Brooklyn; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1923; on the staffs of the Maimonides and Brooklyn hospitals; died May 25, aged 61, of carcinoma of the pancreas.

Smart, James Alexander ⊕ Washington, D. C.; George Washington University School of Medicine, Washington, 1919; specialist certified by the American Board of Otolaryngology; veteran of World War II; for many years associated with the Veterans Administration; died May 30, aged 64, of heart failure.

Smith, Robert Tecumseh ⊕ Nashville, Tenn.; Meharry Medical College, Nashville, 1931; associate professor of medicine at his alma mater; medical director, director of clinics, and chairman of hospital advisory committee, George W. Hubbard Hospital of Meharry Medical College, where he died May 16, aged 58, of pulmonary infarction and arteriosclerotic heart disease.

Smith, Wallace B. ⊕ Fort Worth, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1910; member of the American Academy of General Practice; died May 15, aged 70.

Smolens, Morris S., Levittown, N. Y.; University and Bellevue Hospital Medical College; New York City, 1921; died April 9, aged 61, of coronary artery thrombosis.

Stieglitz, Edward Julius ⊕ Washington, D. C.; born in Chicago June 6, 1899; Rush Medical College, Chicago, 1922; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the American Psychosomatic Society; in 1940 accepted an appointment at the National Institute of Health; on the faculty of the Washington School of Psychiatry; visiting lecturer at the New York University Post-Graduate Medical School and Institute of Industrial Medicine; chairman, Advisory Council on Professional Education, Committee on Chronic Illness; consultant in geriatrics, Veterans Administration; chief of staff of Suburban Hospital in Bethesda, Md.; associated with the Chestnut Lodge Sanitarium in Rockville, Md.; consultant at St. Elizabeth's Hospital and the Washington Home for Incurables; formerly practiced in Chicago, where he was on the faculty of his alma mater, and on the staffs of the Presbyterian, Chicago Memorial, and Chicago Lying-In hospitals; author of books; editor of "Geriatric Medicine"; on the advisory board in geriatrics of the *American Journal of Clinical Nutrition* and on the consulting staff of *Geriatrics*; died in the Suburban Hospital in Bethesda, Md., June 12, aged 58.

Stolpestad, Herbert Lauritz ⊕ St. Paul; University of Minnesota Medical School, Minneapolis, 1934; member of the American Academy of General Practice; veteran of World War II; was shot and killed May 21, aged 50.

Stratford, William Henry, Haw River, N. C.; University College of Medicine, Richmond, 1900; Rush Medical College, Chicago, 1903; for many years practiced in New York City, where he was on the staff of St. Elizabeth's Hospital; died May 16, aged 79, of angina pectoris.

Sullivan, Jeremiah Henry, Rochester, N. Y.; Syracuse University College of Medicine, 1895; an associate member of the American Medical Association; served on the staff of St. Mary's Hospital; died in the Strong Memorial Hospital May 25, aged 89, of arteriosclerotic heart disease.

Tallant, Alice Weld ⊕ Philadelphia; born in Boston July 14, 1875; Johns Hopkins University School of Medicine, Baltimore, 1902; served on the faculty of Woman's Medical College of Pennsylvania; director of the Smith College relief unit in France in 1917-1918; physician of the American Committee on Devastated France in 1919; received the Croix de Guerre from the French government; associated with the Philadelphia General Hospital, the Hospital of the Woman's Medical College of Pennsylvania, and the Woman's Hospital, where she died May 30, aged 82, of circulatory failure.

Templin, Emma L., Hillsboro, Ohio; Woman's Medical College of Cincinnati, 1891; served as a medical missionary in India; died April 17, aged 100.

Tenczar, Francis Joseph ⊕ Chicago; Chicago College of Medicine and Surgery, 1917; member of the American Academy of General Practice; on the staff of St. Mary of Nazareth Hospital; veteran of World War I; died June 15, aged 67, of coronary thrombosis.

Thomas, David Wesley ⊕ Lock Haven, Pa.; born in St. Marys, Pa., in 1886; University of Pennsylvania School of Medicine, Philadelphia, 1912; fellow of the International College of Surgeons and the American College of Surgeons; member of the House of Delegates of the American Medical Association in 1930, 1940, and 1941; past-president of the Medical Society of the State of Pennsylvania and the Clinton County Medical Society, of which he was president and secretary; for many years a member of the board of trustees of the Lock Haven State Teachers College; served as a member of the advisory board to the state department of health; director of the Lock Haven Trust Bank and the Consumer Discount Company; chief surgeon at the Lock Haven Hospital, where he died May 26, aged 72, of congestive heart failure and arteriosclerosis.

Thomas, Emmett Lorin, Cleveland; Maryland College of Eclectic Medicine and Surgery, Baltimore, 1914; Eclectic Medical College, Cincinnati, 1918; on the courtesy staff, Fairview Park Hospital; died May 16, aged 70.

Thompson, Fred Rush, Massillon, Ohio; University of Illinois College of Medicine, Chicago, 1920; assistant superintendent of the Massillon State Hospital; died in the Cleveland Clinic Hospital May 15, aged 64, of carcinoma of the pancreas.

Tillery, Lois Jean, Sonoma, Calif.; University of Washington School of Medicine, Seattle, 1951; interned at the San Diego County General Hospital in San Diego, where she served a residency; on the staff of the Pacific State Hospital in Pomona; died May 25, aged 30, of injuries received in an automobile accident.

Triedman, Harry ⊕ Pawtucket, R. I.; Tufts College Medical School, Boston, 1922; fellow of the International College of Surgeons; examining physician of the Rhode Island Disability Compensation Commission, of which he was one of the organizers; associated with the Miram Hospital in Providence; died May 28, aged 59, of coronary thrombosis.

Tucker, David Andrew Jr. ⊕ Cincinnati; University of Cincinnati College of Medicine, 1916; veteran of World War I; specialist certified by the American Board of Internal Medicine; professor of the history of medicine at his alma mater, where he was assistant to the dean and for many years chairman of the admission committee; fellow of the American College of Physicians; past-president of the Cincinnati Academy of Medicine and the Ohio Academy of Medical History; on the staffs of the Cincinnati General and Christ hospitals; died in the Christian R. Holmes Hospital June 3, aged 67, of multiple myeloma.

Tuthill, Alexander Mackenzie ⊕ Phoenix, Ariz.; born in South Lebanon, N. Y., Sept. 22, 1871; University of Southern California College of Medicine, Los Angeles, 1895; fellow of the American College of Surgeons; past-president of the Maricopa County Medical Society, Greenlee County Medical Society, and the Arizona Medical Association; superintendent of public health in Arizona, 1921-1922; from 1903 to 1916 chief surgeon for the Detroit Copper Company in Morenci; for many years served in the Arizona National Guard, retiring as a major general; served as adjutant general for the state of Arizona and as state director of Civil Defense and of Selective Service; veteran of World War I; member of the Arizona Constitutional Convention; on the staffs of the Memorial, Good Samaritan, and St. Joseph hospitals; died in the Veterans Administration Hospital May 25, aged 86, of arteriosclerosis and nephrosclerosis.

Walcott, William Hunt, Alexandria, Va.; Baltimore Medical College, 1908; formerly health officer of Pittsylvania County, Va., and in charge of a health unit in Carroll County with headquarters in Huntingdon, Tenn.; at one time associated with the U. S. Public Health Service in Washington, D. C.; died May 27, aged 75.

Wallace, Floyd Eldridge ⊕ Chase, Kan.; Kansas City (Mo.) Medical College, 1904; on the staff of St. Rose Hospital in Great Bend; served as mayor of Chase; died in the Grace Hospital, Hutchinson, May 17, aged 78, of cerebral hemorrhage.

Weinberger, Aaron Vida, New York City; University of Louisville (Ky.) Medical Department, 1912; member of the Medical Society of the State of New York; served on the staffs of the Flower and Fifth Avenue hospitals; died in the Hospital for Joint Diseases, June 3, aged 80, of bronchogenic carcinoma.

Wescott, Adeline May, Newburgh, N. Y.; born in 1870; Cornell University Medical College, New York City, 1910; specialist certified by the American Board of Pathology; fellow of the American Psychiatric Association; an associate member of the American Medical Association; served in France during World War I and was associated with the American and French Red Cross and the Rockefeller Foundation; for many years associated with St. Luke's Hospital, where the laboratory was dedicated to her honor as the Adeline M. Wescott Laboratory in recognition of a lifetime of professional service in the field of pathology, and where she died May 19, aged 88, of arteriosclerotic heart disease.

Whinnery, Randall Allan ⊕ Detroit; State University of Iowa College of Medicine, Iowa City, 1938; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; on the staffs of the Florence Crittenden and Harper hospitals; assistant chief of staff, McGregor Center, Hospital for Rehabilitation and Health Education; died in the Jennings Memorial Hospital May 27, aged 47, of lymphoma.

Willour, Leonard Scott, McAlester, Okla.; Medico-Chirurgical College of Philadelphia, 1901; an associate member of the American Medical Association and a member of its House of Delegates in 1920, 1921, and 1926; formerly secretary-treasurer of the Oklahoma State Medical Association of which he was past-president; fellow of the International College of Surgeons and the American College of Surgeons; member of the Oklahoma Historical Society; for many years member of the state board of medical examiners; past-vice-president of the Oklahoma State Society for Crippled Children; veteran of World War I; life member of the Oklahoma Crippled Children's Commission; past-president of the Pittsburg County Medical Society; served as editor of the *Journal of the Oklahoma State Medical Association*; affiliated with McAlester General Hospital and St. Mary's Hospital, where he died May 23, aged 78, of coronary disease.

FOREIGN LETTERS

BRAZIL

Transmission of Toxoplasmosis.—Drs. Ruth S. Nussenweig and Maria B. Deane presented to the Associação Paulista de Medicina the results of their study on the possibility of the transmission of toxoplasmosis through arthropods. They ascertained that Toxoplasma gondii survives for several days in the digestive tract of the triatomids without losing their virulence. Mice inoculated with the triturate or with the contents of the digestive tube of triatomids that had been fed up to three days earlier with infected material died from acute toxoplasmosis, as a rule within 10 days. When the intervals between the infection of the triatomids and the inoculation were longer than five days the results ceased to be dependable. The maximum observed period of survival of the parasite in the arthropod was 12 days. All attempts to transmit toxoplasmosis through interrupted biting or the ingestion of infected triatomids failed. The authors believe that the transmission of toxoplasmosis in nature through biting, feces, or the ingestion of triatomids occurs rarely if at all. Inoculations with eggs from infected triatomids also failed to produce infection. Some of the animals inoculated with material from infected arthropods developed chronic toxoplasmosis. None of the methods used for the diagnosis of chronic toxoplasmosis (subinoculations, search for pseudocysts, Sabin and Feldman's reaction) is completely satisfactory. Only the combined use of all these methods permits the discovery of most cases of chronic infection.

Neonatal Mortality in Premature Infants.—Dr. L. Moura Costa (*Rev. gynec. e obst.* 52:19, 1958) studied the neonatal mortality in premature infants. Of the 25,897 live births occurring at the maternity hospital from June, 1949, to December, 1956, 2,078 or 8% were premature, and of these 250 died in the first month of life, a neonatal mortality of 12%. According to the weight at birth of these infants, the number of deaths and the corresponding neonatal death rates were as follows: 1,000 Gm. (2.2 lb.) or less, 47 infants with 43 deaths, or 91.5%; 1,001 to 1,500 Gm. (2.2 to 3.3 lb.), 127 infants with 82 deaths, or 64.5%; 1,501 to 2,000 Gm. (3.3 to 4.3 lb.), 389 infants with 65 deaths, or 16.7%; and 2,001 to 2,500 Gm. (4.3 to 5.5 lb.), 1,515 infants with 60 deaths, or 4%. There was no significant difference in death rate classified by sex or race. According to the type of delivery, the newborn babies of this series were divided as follows, with their respective neonatal death rates: normal, 1,735 with 195 deaths, or 11.2%; forceps, 160 with 11 deaths, or 7%; cesarean section, 84 with 19 deaths, or 22.6%; and breech, 99 with 25 deaths, or 25.2%. The cause of death could be ascertained by autopsy in only 191 cases. Pneumonopathies accounted for 89 deaths (hyaline membrane 43, intrauterine pneumonia 20, and extrauterine pneumonia 26); anoxia for 34; hemorrhage for 33 (intracranial 13, pulmonary 17, suprarenal 1, and generalized 2); erythroblastosis for 4; congenital malformations for 15 (heart 3, respiratory apparatus 2, genitourinary apparatus 2, digestive apparatus 4, and others 4); prematurity for 5; and undetermined causes for 4. Kernicterus was recognized in seven and syphilis in none.

Topography of the Axillary Vein.—Venipuncture in children is a difficult procedure that can be simplified by using the axillary vein. This problem is particularly important in Brazil where the great frequency of dehydration in children most frequently is met by the use of venous infusions. In order to give the practitioners a good reference to the exact point of passage of the vein under the clavicle, Dr. J. Valle Mendes and co-workers (*Rev. paulista med.* 52:367, 1958) studied 50 fresh cadavers of Brazilians of different racial stocks and varying in age from 0 to 6 years. Observations were carried out on both sides of the body, and thus the data were obtained from 100 measurements. The authors measured the distance between the sternoclavicular and the acromioclavicular joints before the dissection of the infraclavicular region. The same measures were taken after pulling the musculocutaneous layer aside. After the dissection and isolation of the axillary vein the authors observed the passage of this vein beneath the clavicle, measuring the distance between the middle of the anterior surface of the vein and the sternoclavicular joint as well as the diameter of the vessel.

A statistical analysis was made of the data thus obtained in order to estimate the point of passage of the axillary vein under the clavicle, starting from the sternoclavicular joint once the distance between the sternoclavicular and the acromioclavicular joints was known. For this purpose they observed first the two mentioned points, measured on the skin and after dissection, finding no significant differences between the two measurements. The distance between the two joints, measured on the skin, varied from 37 mm. to 96 mm. on the right side, and from 37 to 94 mm. on the left side. The distance between the point of passage of the axillary vein under the clavicle and the middle of the sternoclavicular joint varied from 16 to 38 mm. on the right side and 15 to 37 mm. on the left. With these values the authors constructed a table for the prediction of the wanted distance, which is valid for both sides, as the results obtained on the right side presented no significant difference from those obtained on the left side.

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* The items in these letters are contributed by regular correspondents in the various foreign countries.

DENMARK

School Medical Service.—In Denmark about 650,000 school children are served by 440 school medical officers, about 40 of whom are employed on a full-time basis (*Ugeskrift for læger*, June 12, 1958). In the school year 1955-1956 tuberculin testing continued to yield a fairly constant number of spontaneous positive reactions indicative of some accidental infection, the figure for the first grade in urban schools being 2% as compared with 0.9% for rural schools. This percentage falls with the duration of schooling, being 0.4 in the second and 0.1 in the seventh grade in urban schools. In the first grade 73.5% of the children had been vaccinated with BCG. Smallpox vaccination is so popular that by the time the first school year is reached 96% of the school children have been vaccinated. In this respect rural populations are more enterprising than urban, for in the country only 1.4% of the children in the first grade were not yet vaccinated, whereas the corresponding figure was 5.2% for town-dwellers. By the time the seventh grade was reached, only 0.5% were still unvaccinated. Diphtheria immunization, on the other hand, was more widely practiced in the towns than in the country, the figures being 89 and 73% respectively. The thoroughness with which diphtheria immunization is carried out varied from county to county.

The law enjoins school medical officers to refer all the children with the ailments and anomalies they find to their family physicians. This happened to 20% in the first grade, and thenceforth the percentage fell, with only 10% in the upper grades. A common ailment referable to the family physician was neurosis, which figured more prominently in the urban than in the rural schools. Chronic ear disease showed a much higher rate in urban than in rural areas, but asthma and allied allergic diseases showed no geographical preferences in this respect.

Mistaken Diagnoses of Apoplexy.—During the period 1943 to 1951 the Frederiksberg Hospital had 417 deaths due, according to the clinical diagnosis, to cerebral apoplexy. In 291 of these cases a post-mortem examination was made of the brain. The findings were analyzed by Dr. J. Marquardsen (*Ugeskrift for læger*, May 22, 1958). In 20 patients diffuse cerebral arteriosclerosis was found without definite evidence of focal changes. More disturbing, because of missed opportunities for treatment, were the six patients with chronic subdural hematoma. There were also six patients in whom the correct diagnosis was intracranial tumor. Some of these tumors were malignant gliomas inaccessible to operation. These diagnostic errors were in part due to the advanced age of the patients and the absence of signs of intracranial hypertension. Marquardsen concluded that a safe diagnosis of cerebrovascular accidents can only be established by cerebral angiography, and that when there are no facilities for it the number of mistakes may be reduced by close attention to the course of events and to the mode of development of signs and symptoms. The risk of overlooking a subdural hematoma is particularly great when there has been a high incidence of cerebrovascular incidents.

Suicidal and Accidental Poisonings.—In the fall of 1949 a special center was established in Copenhagen for the care of patients with acute narcotic poisoning. Since then between 800 to 1,000 such patients have been treated every year. Dr. A. Myschetzky (*Danish Medical Bulletin*, May, 1958) studied the records for the five-year period 1952 through 1956 during which 1,762 males and 2,653 females were treated, with a mortality of 4%. About 600 would-be suicides had used more than one agent, a common combination being carbon monoxide and alcohol or some barbiturate. The predominance of the barbiturates over the other toxic agents is emphasized in the fact that they constituted about 72% of all the narcotic poisonings; carbon monoxide was a poor second with about 11%. No less than 30% of the carbon monoxide poisonings must be regarded as unintentional. The motive for attempted suicide was illness in 11%, emotional conflicts in 39%, and economic and social difficulties in 22%. Only 2.6% of the women who attempted suicides gave undesired pregnancy as a motive. With the adoption of new methods of treatment, much has been done to reduce the mortality due to such complications as shock, pneumonia, and renal failure. The mortality from lung complications, for example, fell from 35% in the period 1952-1953 to 17% in the period 1954-1956 with the adoption of massive penicillin doses. The mortality from renal complications fell from 53 to 17%, presumably in response to hemodialysis and levarterenol treatment.

Extrahepatic Operative Lesions of the Biliary Tract.—A series of 18 operative lesions of the biliary tract observed in the Rigshospital in Copenhagen were studied by Dr. Mogens Andreassen (*Ugeskrift for læger*, June 12, 1958). In 5 of these the lesions occurred in this hospital, whereas the remaining 13 were referred to this hospital for lesions originally incurred elsewhere. Three of these lesions followed some operation on the stomach. All the others followed cholecystectomy. Five of the 18 patients died in the operative period, and 13 were discharged in good health. One of these died two years after the last operation, presumably from a new stricture. In the same issue an editorial endorses the modern tendency to be more operation-minded than heretofore in dealing with diseases of the biliary tract, while at the same time facing the disturbing fact that about 1% of all the operations on this tract are complicated by stricture. Perhaps the most important preventive measure is the teaching of junior by senior surgeons never to start an operation in this area without a profound sense of uneasiness over the prospect of this particular disaster.

FINLAND

Rheumatoid Arthritis.—Dr. J. L. Kalliomaki of the University Hospital in Åbo, treated 70 ambulatory patients (54 women and 16 men) who had active rheumatoid arthritis with chloroquine. Each patient received 500 mg. daily during the first week, and then 250 mg. daily. The observation period was one to four months. The reactions to this treatment were classified as subjective or objective (sedimentation rate and hemoglobin level). With regard to the subjective reactions 44 patients noted relief from joint pains, 14 got no relief, and in 12 the pains were worse. The sedimentation rate showed improvement in 43 patients, and the hemoglobin level improved in 34. Leukopenia did not follow in any patient, but four had giddiness, a rash (which may have been due to earlier treatment with gold), and excessive perspiration, although the treatment had to be discontinued on account of side-effects in only two. As this treatment seldom provokes troublesome side-effects, the dosage is simple, and blood counts are not essential. Kalliomaki recommended further trial especially since it is known to be beneficial in systemic lupus erythematosus, which may be present in patients with rheumatoid arthritis.

The Psychic Element in Thyrotoxicosis.—Dr. H. Carpelan (*Nordisk medicin,* June 12, 1958) studied 46 patients (43 women and 3 men) with thyrotoxicosis all of whom had undergone subtotal thyroidectomy. Serving as controls were 26 patients who had undergone thyroidectomy without preoperative hyperthyroidism. Both groups were closely questioned with special reference to psychic factors likely to have provoked thyrotoxicosis. In the first group home conditions when the patient was under 13 years of age were unhappy in 20 (43.5%), whereas they were unhappy in only 4 (15.4%) of the control group. The homes were very poor in 32 (69.5%) of the first group, and in 8 (32.3%) of the controls. In the first group 11 (24%) and in the controls only 1 (3.6%) had been obliged to work for their living before the age of 13. Thus even before puberty the thyrotoxic patient may have had a temporary hyperfunction of the thyroid gland as an adjustment to meet excessive demands.

FRANCE

Pneumoconiosis.—P. Sadoul and co-workers (*Presse méd.* 66:1018, 1958) stated that by means of spirography it is not possible to obtain a complete explanation for the functional disorders found in subjects affected with pneumoconiosis. Even in the absence of an emphysema syndrome a significant diminution in working capacity or even a right heart insufficiency may be present. The authors studied 136 patients with pneumoconiosis, using a spirograph and an ergostat. The patients exercised for 20 minutes only, and in the course of a given exercise the intensity was kept constant. The maximal work tolerated by the pneumoconiotic patient, determined on each by tasks of various intensity, was nearly always found to be less than that tolerated by normal controls. On the other hand, a marked hyperventilation was observed in several silicotic subjects, even during light work. Both phenomena were observed in patients with simple pneumoconiosis as well as in those with silicosis with progressive massive shadows. In certain cases the phenomena could be attributed to an emphysema syndrome, but in others the vascular disorders seemed to be the etiological factor of the abnormalities observed. The role of these vascular disorders was demonstrated by the authors by catheterization of the right heart.

Adenomas of the Hypophysis and Craniopharyngiomas.—J. Decourt and co-workers (*Presse méd.* 66:971, 1958) reported their endocrinological observations of 12 patients with tumor of the hypophysis or the pituitary region (3 with craniopharyngioma and 9 with chromophobe adenoma) and 7 in whom the endocrinological investigations could not be completed owing to the surgical emergency. They demonstrated the value of preoperative hormonal evaluations aiming at detecting any latent adrenal deficiency. Such investigations showed that this deficiency was frequent even though no clinical evidence of hypopituitarism was observed and that insufficiency was largely responsible for the relatively high operative mortality. With the use of preoperative or postoperative corticotherapy it is possible to prevent such accidents. The fact is evidenced by comparing the results of operations performed with or without such treatment.

Procaine.—Michel Pistor (*Presse méd.* 66:999, 1958) studied the action of a complex solution containing procaine as a base and found that the indications for its use were far wider than the simple temporary relief of pain. Procaine in local injections proved markedly effective in such conditions as progressive chronic polyarthritis, astigmatism in children, and aural vertigo (Ménière's syndrome) when combined with vasodilators and certain vitamins that increase the duration of its local action.

Hypoglycemic Coma.—At the December meeting of the Société Médicale des Hôpitaux de Paris R. Weissmann and co-workers cited a case of hypoglycemic coma that occurred on the fifth day of treatment with carbutamide. On the first day the patient took nine tablets and on the second day he showed evidences of hypoglycemia. After he had taken 13 tablets (6.5 Gm.) he developed coma, fever, dyspnea, and a positive Babinski's sign. At first a cerebrovascular accident was suspected.

Revascularization of Myocardium.—N. Hortolomei and co-workers (*Lyon Chirurgical,* Jan., 1958) made a direct anastomosis of the internal mammary and coronary arteries in 10 dogs. Of these seven died in ventricular fibrillation, one of thrombosis of the mammary vein five days later, and one after a month of empyema. The one that lived was in excellent health after 18 months. He was killed, and the myocardium showed a good nutritional state. The chief operative difficulty consists in trying to suture small vessels with the heart in movement.

Encopresis.—J. Duhamel and co-workers (*Archives françaises de pédiatrie,* no. 10, 1957) studied a series of 33 children (31 boys and 2 girls) with encopresis. All were over 2 years old. None had any organic disease. According to the authors encopresis is not a disease of the anal sphincter but of the voluntary command of the sphincter. Mentally the children were normal, but they showed evidence of neglect, emotional instability, sexual preoccupation, a tendency to be dirty, and lack of self-reliance. On the contrary the parents showed a tendency to supercleanliness, anxiety, and preoccupation with intestinal function. The only treatment of any value was to overcome the emotional conflict between the child and parents.

INDIA

Treatment of Leukemia.—Dube and Srivastava (*J. Indian M. A.* 30:10 [May 16] 1958) treated 15 patients with chronic and 5 with acute granulocytic leukemia with desacetylmethylcolchicine. The drug is believed to have a selective depressant action on granulocytes and to increase red blood cells, hemoglobin, and platelets. Of the 15 with chronic leukemia, 2 had had a course of deep x-ray therapy one year earlier and 2 others had become resistant to treatment with busulfan. The rest had received no previous treatment. Therapy was started with 1 mg. of the drug three times a day for 4 days. The dose was then increased gradually by 2 mg. a day till a total of 8 mg. a day was reached. This dose was continued till the total leukocyte count came down to 20,000. Therapy with the drug was then stopped for three days after which a maintenance dose of 3 mg. a day was given. No significant beneficial effects were seen in the patients with acute leukemia. Only two showed any response. In these the leukocyte count was markedly reduced, the bone marrow showed an increased number of mature cells, and there was some clinical improvement. This remission lasted only one to three months.

All the patients with chronic leukemia, however, showed marked clinical improvement, with reduction in the size of the spleen, which became barely palpable in most of them after one to one and one-half months' treatment. In several patients, there was complete disappearance of immature cells from the peripheral blood while the total erythrocyte count, hemoglobin level, and platelet count showed a marked increase. In some patients the peripheral blood findings returned to normal. Examination of bone marrow showed reduced cellularity with fewer premyelocytes and myelocytes, but the general findings were similar to those of chonic granulocytic leukemia. On an average about 6 to 8 mg. a day of the drug for 10 to 20 days were required to cause reduction in the total leukocyte count. If the maintenance dose had to be discontinued, there was a tendency for the leukocyte count to go up again. In the present series the patients when last seen had remained well over a period of 14 months without a remission on therapy with the maintenance dose which was being continued. There were no toxic effects except in one patient who developed severe toxemia with leukopenia. He responded to citrovorum factor with excellent results. Thus the results were encouraging in patients with chronic granulocytic leukemia, but in those with the acute form, it failed to produce any lasting benefit.

Family Planning.—The family planning program is being intensified after an encouraging response from the people and an increasing awareness of the necessity of family limitation. Family planning is being made an integral part of the services in about 600 district hospitals, 1,500 subdivision hospitals, and 1,100 health centers. By March, 1958, the number of urban clinics opened was 176 and the number of rural clinics opened was 309. The people in villages have begun to take the program seriously. Between 60 and 80% of the women in the Ludhiana and Ramanagaram rural experimental centers favor planned parenthood. As shortage of trained personnel is the main deterrent to an all-out family planning program, more training centers are being opened and several training teams consisting of a doctor and social workers are touring the villages. The number of persons trained at the Bombay family planning training and research center and the Ramanagaram demonstration and experimental center in the year 1957-1958 was 293. The approach of family planning workers in the rural areas is also being reoriented. While laying their main emphasis on the family planning program, these workers also assist families in other welfare activities. Linked to the question of family planning are the issues of legalizing abortions and sterilization. All possibility of legalizing abortions is ruled out on moral and health grounds. The government's attitude to sterilization is that it should be encouraged in suitable cases with the consent of both the husband and the wife. The Madras Government has set the pace by providing facilities for sterilizing men.

Tropical Eosinophilia.—B. S. Raheja (*J. Indian M. A.* 30:10 [May 16] 1958) stated that although organic arsenical preparations have been regarded as more or less specific in the treatment of tropical eosinophilia, some patients fail to respond to these drugs and others cannot take arsenic in even the smallest doses. For such patients, diethylcarbamazine was tried by other physicians with good results. The author treated 34 patients who had tropical eosinophilia with diethylcarbamazine, and of these 32 were cured. These patients presented the typical clinical findings of tropical eosinophilia with total circulating eosinophil counts of over 2,000 per cubic millimeter. The dosage was calculated on the basis of 13 mg. per kilogram of body weight spread over four days and administered in three equal daily doses. Two patients had been previously treated with chlortetracycline with no improvement, one had had ACTH, and another prednisone with partial temporary relief. Five also had ascariasis, and one had vegetative forms of Entamoeba histolytica in the stool; two had hypertension; one had diabetes; and one was pregnant. The youngest was 6 and the oldest 56; 13 had suffered from previous attacks sometime in the preceding seven years, and 7 of these were intolerant to arsenic. The highest eosinophil count met with in this series was 34,960 and the lowest 2,106 per cubic millimeter. The percentage of eosinophils varied between 19 and 81. The degree of eosinophilia had no relation to the intensity or severity of the clinical condition. Similarly, the clinical improvement and reduction in the number of circulating eosinophils after treatment showed no correlation, the latter sometimes taking much longer to return to normal. Of the two failures in the series, one also had amebiasis and was relieved after antiamebic treatment. In the rest, relief was noted between the second and eighth day of treatment and complete cure between the 4th and 16th day. No serious side-effects or untoward reactions were seen, but some complained of giddiness or drowsiness. One patient developed leukopenia which persisted for three months.

New Radioactive Cobalt Unit.—The Chittaranjan Cancer Hospital, Calcutta, is getting a radioactive cobalt (Co^{60}) unit from Canada, the first of its kind in India. It will be installed and maintained by the International General Electric Company. A special room was built to house the unit.

Pentamethylenetetrazol-Induced Seizure.—N. Das and co-workers (*Calcutta M. J.* 55:4 [April] 1958) studied the comparative action of reserpine and phenobarbital regarding the electrical activity of brain and behavioral changes in rabbits. Nonanesthetized animals were used for these experiments. Seizures were induced with intravenous injections of 10 mg. of pentamethylenetetrazol per kilogram of body weight. A 2% solution of phenobarbital and a 1:1,000 solution of reserpine were used as anticonvulsants. Pentamethylenetetrazol injections consistently produced convulsive states including tonic and clonic phases as shown by behavioral and electroencephalographic changes. When a previous injection of phenobarbital was given, these convulsion-inducing properties were modified or inhibited in almost all the rabbits. It also exerted a hypnotic or narcotic effect which was manifested by the sleep pattern in the electroencephalogram. The effect of phenobarbital persisted for 24 to 48 hours.

Reserpine was given intravenously in a single dose varying from 0.1 to 1 mg. per kg. With 0.3 mg. per kilogram of the drug, within 40 to 50 minutes, a sedative effect was produced, the animal losing interest in its surroundings although it could be aroused by sound and tactile stimuli. The electroencephalogram showed a diminution in the voltage of the brain waves. With double this dose, the animals were even less alert and did not respond to sound or touch, while changes in the electroencephalogram were more marked, but there was no evidence of sleep. The effect was more of a tranquilizing and inactivating nature without inducing sleep. The effects were more severe with a dose of 1 mg. per kilogram. The animals were completely relaxed with abolition of some peripheral reflexes, shallow respiration, and a slow, weak pulse. The electroencephalogram showed slowing and flattening of the waves with maximal reduction in the voltage of waves from the occipital areas. With 0.3 mg. per kilogram, there was hardly any anticonvulsant effect; with 0.6 mg. per kilogram the convulsion-inducing property of the drug was modified and the latent period was prolonged in some animals; and with 1 mg. per kilogram the intensity of the seizures was diminished and their appearance in the electroencephalogram was checked completely. The effect of the drug continued for 12 to 36 hours.

Eradication of Malaria.—Work has begun throughout India on the eradication of malaria. The plan seeks to eliminate the malaria parasite in six years by the radical cure of every malaria patient. At the end of this period it is hoped that everyone will be free from the infection. The malaria-carrying mosquito will then be rendered harmless. The mosquito has been the target of attack in malaria control measures taken so far. The strategy of the new campaign is to destroy the malaria parasite living or lying dormant in the blood stream. Sharing in the bid to rid India of the scourge are the government of India, the state governments, and the Technical Cooperation Mission of the United States government. Malaria eradication programs are being undertaken on a global basis. Among the countries in the East, India has taken the lead in the present campaign. Experts regard the present time opportune for a change of tactics in the fight against malaria. The spraying of DDT to destroy vector mosquitoes has undoubtedly yielded spectacular results and reduced the incidence of malaria, but, in some countries, the constant use of DDT has produced DDT-resistant strains of mosquitoes.

The new six-year program includes an intensification of DDT spraying to reduce the incidence of malaria to a minimum and the launching of a house-to-house surveillance for detecting and curing every malaria patient so that he ceases to be a source of infection. The country-wide surveillance will begin at the end of the second year and will be maintained for the following four years. To detect cases of fever, 100 investigators will be appointed for every million persons. Each investigator will be responsible for a group of about 2,000 houses. It will be his duty to visit them every fortnight and make inquiries. When a case of fever is detected, the investigator will collect a blood smear of the patient and send the slide to the laboratory. If malaria parasites are found, the patient will be given intensive treatment, to be continued until he is free from the malaria parasites. The insecticide equipment and the vehicles necessary to implement the scheme will be supplied by the U. S. Government under the Indo–United States technical assistance agreement. The government of India will share half the increased costs on the additional work with the various state governments and also increase the staff at the Malaria Institute of India both for supervision in the field and for training new personnel.

Cervical Cord Compression.—Ramamurthi and Jagannathan (*Neurology* 6:1, Jan.-March 1958) reported a series of 19 patients with nontraumatic cervical cord compression. These included five with extradural tumor (one with malignant osteoclastoma, one with sympathicoblastoma, one with tuberculoma, one with osteitis deformans, and one with a central massive herniation of the nucleus pulposus); 8 with intradural lesion (3 with neurofibroma, one with meningioma, and 4 with arachnitis); 4 with intramedullary tumors (three with ependymomas and one with syringomyelia); and 2 in whom the cause was not determined. The cervical cord was affected second in frequency, considering compression at all levels of the spinal cord. In four patients motor symptoms caused by anterior cord compression in the early stages predominated and were diagnosed mistakenly as due to amyotrophic lateral sclerosis. Two patients were being treated initially as having primary brachial neuritis because they had radiating pain along the arm. In one patient, temporary remission of symptoms occurred leading to the erroneous diagnosis of multiple sclerosis. All patients had a lumbar puncture.

Partial block was common in the cervical region, as the canal here is wide, and partial block should therefore be detected by plotting the rate of fall of the level of the spinal fluid after jugular compression for 10 seconds. Protein levels in the spinal fluid were not usually high in patients with cervical cord compression as compared with those having tumors lower down, and the average protein content in these patients was 80 mg. per 100 ml. Getting a cisternal myelogram might not be a safe procedure or even possible in the presence of a high cervical lesion. In such a case a lumbar myelogram was made, while in those with a low cervical lesion a cisternal myelogram was made. Screening in myelography was done to detect partial blocks. Excessive flexion of the neck during operation to get better exposure should be avoided, as it may cause permanent damage to the cord resulting in death, as happened in one patient whose cord was already kinked. In patients with lesions situated anterior to the dura mater, the authors found it easier to incise the dura posteriorly, gently retract the cord, incise the dura anteriorly, and remove the tumor intradurally. In those with intramedullary lesions, the cord was cut in the center in the posterior midline and the tumor was removed. This was done in three patients with intramedullary ependymoma who did well.

The chief complication in the postoperative period was respiratory difficulty, and patients had sometimes to be put in the iron lung for 48 to 72 hours. One patient with osteitis deformans of the axis, in whom the cord was already kinked and was probably damaged during operation, died after three days without recovering his power of respiration. Such complications as fever and acute dilatation of the stomach were not met with in this series. The cervical spine was not fused in any of these patients. One of those with neurofibroma developed encysting of the spinal fluid postoperatively, which formed a swelling under the scar. This gradually disappeared after 12 weeks. Two patients died in the immediate postoperative period, one of respiratory failure and one of a cerebrospinal fluid leak that became infected. Patients having their symptoms for a long time preoperatively recovered slowly even after complete decompression. One intramedullary ependymoma recurred four years after operation, and the patient died six months after reoperation.

Vaginal Cytology and Sterility.—S. N. Mukherjee (*Calcutta M. J.* 55:4 [April] 1958) studied vaginal smears in 35 women with normal fertility, 83 with primary sterility, and 20 with secondary sterility. The curve of cornification of vaginal epithelial cells followed a definite pattern in fertile women, showing a peak near the midcycle with low values at the beginning and end of the menstrual cycle. The same pattern was also observed in both sterile groups. The percentage of cornified cells was, however, significantly higher in the normal group than in those with primary sterility in all the phases of the cycle except the first. In those with secondary sterility, the difference in percentage assumed statistical significance only in the midcycle, being higher in the normal group. The curves of intermediate cells in the vaginal smears also followed a distinct pattern, with lowest values near the midcycle and higher values in the beginning and end of the cycle in all the three groups. The percentage of these cells was lower in the fertile group during the middle of the cycle as compared with the other two groups, while it was higher than that in the primary sterile group in the late luteal and premenstrual phase.

Studies on basal body temperature records in the three groups revealed the typical biphasic variation in 74%. In 80% the records presented sufficient data to reflect the ovarian function. Estimations of vaginal glycogen showed that the concentration increased about the midcycle in 80% of the subjects of the normal group, showing lower values during the beginning and end of the cycle and higher values in midcycle, as compared to the primary sterile group; 75% of all the subjects revealed a periodic fluctuation of the pH values in different periods of the menstrual cycle; 65.6% of these showed a definite pattern of ovulatory pH curve with the lowest value near the midcycle and higher values at the beginning and end of the cycle. The pH was lower in the normal group in the preovulatory phase and higher in the premenstrual phase as compared with the sterile groups. The incidence of anovular cycles was 6.6% in the sterile groups, while the normal group did not show a single anovular cycle. These studies on vaginal smears supplemented with basal temperature records, vaginal glycogen, pH values, and endometrial biopsy were of value in interpreting ovarian function and the occurrence of ovulation. With the help of these investigations, patients with functional sterility were classified into those with (1) anovular cycles; (2) inadequacy of both estrogen and progesterone; (3) inadequate luteal phase only; and (4) pathological endometrium. It also helped to differentiate between estrogen and progesterone deficiency, in assessing the nature of ovarian function and locating the time of ovulation. It helped in determining the endocrine status and the presence or absence of ovulation in patients with sterility in whom no organic cause could be detected.

PERU

Herniation of the Nucleus Pulposus.—At the 11th Peruvian Congress of Surgery in April in Lima Dr. J. Franco of Lima reported that in a series of 574 patients with herniation of the nucleus pulposus 416 (73%) were treated surgically. It has become clear that surgery should be reserved for those who are incapacitated by repeated attacks of severe sciatic pain and in whom conservative measures have failed to bring consistent relief. The mainstays of medical management are: (1) rest on a firm bed, (2) muscle-relaxing drugs, (3) proper postural and corrective exercises, (4) cortisone-like steroids, given by conventional routes and even intrathecally, in properly selected cases, and (5) hydrotherapy, diathermy, and ultrasound waves.

Dr. E. Sabogal discussed the aforementioned 416 patients who were operated on. A total of 463 protruded disks were removed from these patients. Males accounted for 88.8% of the series; 13 patients were between 10 and 20 years of age; 137 between 21 and 30; 131 between 31 and 40; 95 between 41 and 50; 37 between 51 and 60; and only 3 were over 60. In 98.3%, the herniated disks were located in the lumbar spine; they were in the cervical spine in five patients and in the thoracic spine in two. The herniated nucleus pulposus involved the fourth lumbar intervertebral disk in about a half of the patients. In 42 patients there were multiple herniations, and in 33 of these the correct diagnosis was made by myelography prior to operation. Single protruded disks were demonstrated by myelography in all the other patients. After discharge, 141 patients had a recurrence of symptoms. Of these, 105 were treated medically on an ambulatory basis and made a complete recovery. The remaining 36 had to be hospitalized again. Overlooked herniated disks in adjacent intervertebral spaces and inadequate operative evacuation of the disk were demonstrated in nine and two patients respectively. In 16 neither of these conditions was found and the pain was controlled by medical means only. The following complications were observed: spondylitis in three, postoperative fistula in three, and tibial nerve paralysis in one. No operative death occurred. Final results were classed as excellent in 275 patients (66.1%); fair in 134 (32.2%); and poor in the 7 (1.7%) with postoperative complications.

Dr. L. Quiñones reported on the histological characteristics of 98 of the aforementioned disks removed. He found that 47 of these were normal. A large proportion of the pathological disks came from patients with a short clinical course. There was no significant relationship between the state of the disk and the nature or intensity of the symptoms.

Professor E. Rocca of Lima said that myelography and diskography are of great value in the diagnosis of intervertebral disk herniation and that characteristic sciatic pain may be elicited also by having the patient walk on either toes or heels only. He urged the study of the muscular chronaxy as a further procedure of great usefulness in the diagnosis of lumbago-sciatica.

Drs. G. Costa and D. Morote stated that determination of the muscle chronaxy should be made in every case of clinically suspected herniation of the nucleus pulposus. They performed this study in 41 patients of the aforementioned series and found that unilateral or bilateral nerve root lesion existed in 28 of them. In comparison only 27 of the same group had typical sciatic pain, 18 had abnormal reflexes, 16 had pain after leg-straightening maneuvers, and 13 had sensory changes. Only lumbar pain was present in a larger percentage (80.8) of the patients than was abnormal chronaxy. Studies of chronaxy were useful in the diagnosis of the syndrome, but they were worthless in the topographic diagnosis of the herniation. On the other hand, abnormally high values of chronaxy were found to be related to both the duration of the disease and the intensity of the nerve root compression.

Spondyloarthritis.—At the same meeting Dr. G. Córdova said that in spondyloarthritis, after an asymptomatic period, vague symptoms appear. Pain and muscle spasm in variable degrees are the most prominent of these symptoms. Late in the course of the disease atrophy, sympathetic disturbances, and diverse systemic changes arise. The roentgenographic findings are characteristic. Frequently, however, no relationship is found between them and the clinical manifestations. Changes in the spine compatible with this condition in apparently healthy subjects with no previous history of back pain have been found both on radiologic and postmortem studies. The speaker studied roentgenograms of the spine in a group of 100 healthy persons aged between 40 and 60 who had no history of pain in or trauma to the spine and found that 21% had mild arthritic lesions, the age of these subjects ranging from 40 to 50, and that 44% showed rather advanced lesions, their ages being between 50 and 60.

On the other hand, the author reported on a series of 185 patients with this disease treated in the Loayza Hospital in Lima. This figure represented 16% of the patients with disease of the spinal column seen during the review period. Their ages ranged from 30 to 85 years, with a peak incidence in the age group 51 to 60 years, which accounted for 65 of the patients (35%). The lumbar spine was involved in 91 patients (49%), the thoracic spine in 40 (21.5%), the thoracic and lumbar spine in 37 (20%), the lumbar and sacral spine in 12 (7%), and the cervical spine in 5 (2.5%). In 91% typical localized pain, muscle spasm, and limitation of function were present. In most patients the pain radiated to a limb and/or was associated with aching in the adjacent organs. This caused diagnostic difficulties in some patients. The roentgenograms revealed typical advanced lesions in 137 (74.5%), mild lesions in 41 (22%), and no apparent lesions in 7 (3.5%). Of 120 patients who underwent both medical and orthopedic management, a follow-up showed that 28 were free of symptoms, 60 obtained marked relief and were working, 7 were not improved, and 25 could not be located. Medical therapy only was given to 39 patients. Results considered as satisfactory were obtained in 14 of them, and the remainder were not contacted. Roentgentherapy was used in 10 patients. Of these three obtained complete relief, four obtained marked improvement, and three could not be located. Procaine solution was given intravenously to 16 patients. Of these 11 got relief from pain and 5 had no improvement. The speaker concluded that the best treatment for the control of the pain is rest on firm bed and diathermy, the effects of both these measures being greater and more lasting when factors aggravating the condition could be removed.

Surgery of the Colon.—At the same meeting Dr. A. Sabogal reported on 85 patients with rectosigmoid cancer, 3 with anorectal melanoma, and one with reticular cell sarcoma of the rectum treated in the National Institute of Neoplastic Diseases at Lima. The value of rectal digital examination was stressed. This should always be supplemented with proctoscopic and radiologic examination and biopsy. In this series 76% of the cancers were adenocarcinomas. Up to 13% of the patients had been given a diagnosis of hemorrhoids one to five months prior to their admission to the institute, where the correct diagnosis was finally reached; 66% of the cases occurred in women, and the age group most affected was that between 50 and 70. In general, the patients with rectosigmoid cancer tended to seek medical advice earlier than did those with cancer at the rectal ampulla. The condition in 25% of the patients was inoperable; a radical operation was performed in 42%; and a palliative operation was performed in the remaining 33%. The operative death rate was 6.8%, and 33.2% showed a postoperative survival of three years or more.

Dr. R. Pinillos said that diverticulosis of the colon was present in 80 to 90% of the persons in the oldest age groups. In the general population exceeding 50 years it was found in 7 to 10 of every 100 autopsies. Diverticulosis was not troublesome in itself, but 20% of these patients developed the so-called diverticulitis of varying severity. In rare cases malignant degeneration also occurred. No pathogenic relationship has been proved between diverticulosis and cancer, but in elderly patients these conditions may coexist. The clinical course of diverticulitis is variable, and symptoms most frequently resemble a subacute appendicitis on the left side. Diffuse or localized peritonitis may eventually result. Medical management consists of a suitable diet and prompt, rigid treatment of the intestinal infections. In diverticulitis surgery is indicated only after the infection has been controlled medically, unless a severe complication that requires immediate operation arises.

Dr. L. Gurmendi reported a series of 40 patients with volvulus of the sigmoid flexure. Most of the patients were between 20 and 30 years old; 36 were women and 4 were men. In 22 patients the volvulus was acute, and in 18 it was chronic. Abdominal pain was present in 37, localized abdominal distention in 32, constipation in 31, inability to pass flatus in 30, nausea in 29, vomiting in 26, tachycardia in 25, and Kussmaul's sign in 18. Every patient with acute volvulus should be operated on. The speaker preferred primary resection with end-to-end anastomosis. There were eight deaths in this series.

UNITED KINGDOM

Irradiation Laboratory.—A new irradiation laboratory housing a linear accelerator was opened by the Metropolitan-Vickers Electrical Engineering Company of Manchester. This company has done much basic research leading to the construction of the linear particle accelerator, a device in which a stream of particles traveling in a hollow wave guide is accelerated by a radio frequency field, forming a source of highly concentrated focused x-rays. The accelerator, besides providing the most modern radiotherapy treatment for cancer, has industrial uses, and it is for such a purpose that the new linear accelerator has been built. Metropolitan-Vickers are offering it as a service to industry for the large-scale sterilizing of pharmaceutical products and foodstuffs, particularly when these are thermolabile. This cold sterilization kills organisms without any appreciable rise in temperature of the medium. Penicillin and sutures, for example, can be sterilized by means of the linear accelerator, and a large number of drugs given parenterally can be treated by it. Insulin, however, undergoes some molecular change with loss of potency, probably due to polymerization. Advantage of the polymerizing effect of irradiation can be taken in the manufacture of dextran by tailoring the molecule to correspond physically with the properties of plasma. One advantage of sterilization by the linear accelerator is that it can be applied on a large scale and at low cost. The outside maintenance cost of the installation is not more than $3,000 a year, or about $6 an hour of actual running time. The rental charge of the installation is likely to be about $140 a day. The processing of ampuls and vials is estimated to cost $1.40 per pound.

Leprosarium in Nyasaland.—The Federal Ministry of Health of Nyasaland has established a new leprosarium and hospital at Kochira costing about $220,000, as a step toward the treatment and eradication of leprosy in the country. The settlement consists of a central hospital and 120 houses, each of which will accommodate four patients. A recent survey by a leading leprologist drew attention to the high incidence of leprosy in the protectorate and recommended the establishment of the leprosarium, with facilities for inpatient, residential, and outpatient treatment. The British Leprosy Relief Association recruited a trained leprosy worker to act as superintendent of the settlement.

Doctors' Prospects.—The Council of the British Medical Association submitted a second supplementary memorandum to the Royal Commission on Doctors' Remuneration. It stated that competition for specialist posts in hospitals is very keen. Many who attempt to qualify reach the age of 40 without having attained appointments as specialists. This is often through no fault of the physician but because the National Health Service has encouraged young men and women to train without having enough appointments for them at the end of their training. A drastic overhaul of the structure of medical staffing of hospitals is long overdue. There is now difficulty in obtaining junior staff because they are underpaid and their prospects are poor. They may rise to the position of senior resident, and there they often remain with little hope of advancement. Owing to the uncertain and unattractive prospects of a career in the National Health Service hospitals a number of able and promising physicians have emigrated.

Even if the hospital doctor achieves specialist status he finds that private practice has dwindled and that the financial rewards, except to the well-established specialist, are comparatively small. The council points out that the Spens Committee recommended that all specialists, whether full-time or part-time in the health service, should be paid expenses incurred in addition to their remuneration. This has never been done, nor have full-time specialists been allowed to obtain a tax rebate on their expenses. Only part-time specialists are allowed this. On the other hand many of the latter have insufficient paid hospital work and are unable to make up the balance by private practice. Both groups of specialists are underpaid according to the council's memorandum, which stated that at best the basic salary scale of specialists in the hospital service today can only be regarded as representing 1951 values of money. It recommended a basic incremental scale for hospital specialists of at least 29% above present values and an increase of 60% for their domiciliary consultation fees, which have remained the same since 1948. The so-called merit or distinction awards received by 34% of hospital specialists have never been raised, and the council recommend that these should also be increased by 60%. Their final recommendation on specialist's remuneration is a scale rising from $7,587 to $11,240 annually by annual increments of $457. The three grades of distinction award recommended by the council are: first grade $2,250, second grade $6,785, and third grade $11,250. These would be received by 20%, 10%, and 4% of specialists respectively.

The council was also concerned at the low rates of remuneration of other hospital staff. When the National Health Service started a new hospital grade was introduced, the so-called senior hospital medical officer, of status between that of resident and specialist. Many of these never received promotion to full specialist status, although their experience and qualifications usually warrant this. The hospital authorities are thus obtaining specialist service for less than specialist pay. Assuming appointment at the age of 32, a specialist on the basic scale earns $93,362 more than his senior hospital medical officer colleague by the time he retires. As the status, ability, and responsibility of the latter approximate to that of the specialist, the council recommends that the salary of the senior hospital medical officer should be at least 80% of that of the basic specialist scale. This would be a more realistic evaluation of the work which they are doing in the health service. Their recommended salary scale is $6,060 to $9,000 annually, with increments of $365. The council also recommended an increase in the present salary scales of other hospital physicians of about 50% and adequate expense allowances, which should also be recognized for tax purposes. At present full-time medical staff in the hospital service are neither reimbursed nor allowed tax remission for professional expenses.

Insulin Treatment of Schizophrenia.—Since the introduction of the insulin treatment of schizophrenia no comparison was made between the results obtained by this method and by the intravenous injection of dextrose without insulin. This has now been made by Dr. Sheila Leyton (*Lancet* 1:1253, 1956). Patients referred to the insulin treatment unit of a mental hospital were divided, by alternate selection, into two roughly similar groups, the first receiving insulin hypoglycemia and dextrose, while the other had dextrose alone. The insulin treatment was given on customary lines, the hypoglycemia being terminated by the intravenous injection of 40 to 60 ml. of 33% dextrose, followed by sugar given orally. The patients in the dextrose control group were given daily injections of sterile water and flavored sugar drinks for the first week and 20 ml. of dextrose per day intravenously followed by a drink in the second week. The amount of dextrose was increased to 40 ml. in the third week and 60 ml. in the fourth week. Patients in both groups had 40 to 50 injections, with the occurrence of coma in about 40 in the insulin-treated group. Both groups were treated in the same way from the point of view of diet, occupational and social activities, and attention from the nursing and medical staff. The results of the trial were assessed by the discharge rate of the patients. There was no significant difference between the rates for the two groups.

The Nipple in Pregnancy.—The value of routine preparation of breasts and nipples during pregnancy, with a view to improving the prospects of breast feeding, is dubious, and the anatomic improvements claimed for such treatment are probably due, in most women, to normal physiological changes during pregnancy, according to Hyten and Baird (*Lancet* 1:1201, 1958) who studied the nipples of 170 primigravidas and 104 multigravidas from early pregnancy until the puerperium. No antenatal treatment was given to defective nipples. The nipples of about 33% of the primigravidas were judged to be defective, on ground of retraction or poor protraction in early pregnancy, but only about 8% were judged to have defective nipples in the puerperium. In second pregnancies the proportions were 10% in early pregnancy and 4% in the puerperium. In third and subsequent pregnancies none of the women examined had defective nipples. The assessment of nipples in early pregnancy gave only limited help in predicting which women would experience difficulty with breast feeding due to inadequacy of the nipples. In any case, this kind of difficulty is relatively uncommon, occurring in less than 5% of primigravidas and less than 2% of multiparas who start breast feeding.

CORRESPONDENCE

HYPERBILIRUBINEMIA IN INFANTS

To the Editor:—Recently we became aware of an association between the administration of large amounts (72 mg.) of a vitamin K analogue, menadione sodium bisulfite (Hykinone), intravenously to mothers in labor and the occurrence of marked, early hyperbilirubinemia in newborn premature infants. We have encountered seven such cases, the details of which are listed in the table. These infants were first noted to have markedly elevated levels of serum bilirubin between 40-72 hours of age. All but one were treated with exchange transfusion in an effort to prevent neurological damage (kernicterus) from the hyperbilirubinemia. Under ordinary conditions jaundice of this degree does not occur until the fourth to sixth day of life.

Data Relative to Administration of Menadione Sodium Bisulfite in Seven Infants

		Blood Group of		Dosage				
Case	Weight, Gm.	Infant	Mother	Amount, Mg.	Route	Hours Prior to Delivery	Highest Billirubin level (Mg %)	Follow up
1	1,575	O-	O-	72	Im	112	35	Died: kernicterus
2	2,353	O+	B+	72	Iv	34	21	Normal at age 1 year
3	1,680	A+	AB+	72	Im	10	25	Normal at age 11 months
4	1,530	B+	B+	72	Iv	5	26	Died at age 1 month: liver abscess: sepsis
5	1,431	A+	A+	72	Iv	24	28	Normal at age 9 months
6	2,013	A+	O+	72	Iv	2	46	Normal at age 6 months
7	2,792	O+	O+	72	Iv	3	47	Retarded development

There is adequate evidence in the literature to show that vitamin K analogues are capable of causing hyperbilirubinemia when administered in large amounts to premature infants. Inasmuch as doses as small as 1-10 mg. given by mouth to the mother ante partum have been shown to have an effect upon the prothrombin time of infants on the third day of life, the intravenous administration of a large amount of a water-soluble, low-molecular-weight compound such as menadione sodium bisulfite probably enhances the amount getting to the fetus. Because of the risk involved we feel that there are no indications for the routine administration of large amounts of menadione sodium bisulfite ante partum and that it is a practice which should be discontinued. A more detailed report of this study will be published. In the interim we would appreciate hearing from other doctors who may have had similar experience.

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BANANAS IN THE DIET AS A CAUSE FOR FALSE-POSITIVE REACTION FOR OCCULT BLOOD IN THE STOOL

To the Editor:—Bananas are widely eaten by patients and wisely recommended by physicians in many diverse medical conditions because of their easy digestibility, welcome palatability, and excellent nutritional value. Due to these features plus their satisfying bulk, several bananas daily are not infrequently eaten by patients placed on a meat-free diet to obtain stool for occult blood determination.

A patient with unexplained secondary anemia was placed on the usual meat-free diet to determine whether there was gastrointestinal bleeding. After four days, the stool was tested for occult blood by the usual benzidine reaction method, and the result was positive. When the patient commented that her gastritis was much improved by her "banana diet," my interest was aroused by this fact and also by the possible effect of a "banana diet" on the test. After she stopped eating three to five bananas daily, the test became negative. With bananas included again, the test again became positive.

On checking with several colleagues, I found that a few were familiar with the fact I had uncovered, but I was amazed at the number of experienced physicians not familiar with this useful "pearl" of knowledge.

The peroxidase enzyme responsible for the positive test reaction is present in much higher concentration in potatoes than in bananas, but it is destroyed in cooking. In bananas the concentration is apparently enough that if they are eaten in any quantity, a positive reaction may be obtained.

In conclusion, bananas in the diet may produce a false-positive reaction in the stool test for occult blood when one of the usual tests based on the peroxidase reaction is employed.

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MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Etiology of Hemochromatosis Not Due to Transfusion: Review of the Question: Study of Heredity in 21 Families. J. Pirart and P. Gatez. Semaine hôp. Paris 34:1044-1051 (April 12) 1958 (In French) [Paris].

Idiopathic hemochromatosis occurs as a congenital and hereditary biochemical disorder. Nevertheless, certain acquired conditions must also be retained as causes of the disease or at least as factors contributing to its development. Notable among these are malnutrition, alcoholism, hepatitis, and chronic anemia. Alcoholism, found in 19 of the patients in this study, sometimes plays the part of a revelatory factor by aggravating cirrhosis already present as a result of the underlying hemosiderosis. Again, alcoholic cirrhosis and hemochromatosis may occur fortuitously in the same patient and may be discovered simultaneously by an artefact of detection.

Acquired conditions, however, are absent in some cases of hemochromatosis, and in these the causal significance of hereditary factors is becoming increasingly clear. These factors were studied in 50 patients with idiopathic hemochromatosis who belonged to 46 families, 21 of which were investigated in detail. Estimates of serum iron and, usually, a test of provoked hypersideremia were made in 36 subjects. The coexistence of melanodermia, hypertrophic cirrhosis, hypogenitalism, and even diabetes does not in itself suffice to establish a diagnosis of hemochromatosis. Such a diagnosis, in fact, must be supported by the discovery of large deposits of hemosiderin in the liver, and also perhaps in the skin or the bone marrow, in the absence of any hemolytic disease.

The conditions found in close relatives of the various propositi in this series included 3 cases of diabetes; 4 cases of complete hemochromatosis, 2 of which were proved; 6 cases of subclinical incomplete hemochromatosis, 1 of which was proved; and several cases of ordinary melanodermia distributed among the members of 11 families. Preclinical, biochemical hemochromatosis was found in 13 patients, in 3 of whom it was demonstrated both by punch biopsy of the liver and by the bleeding test. These 3 patients have undergone repeated bleedings resulting in the withdrawal of 13, 13.5, and 15 liters of blood, respectively, during a 2½-year period without showing the slightest evidence of anemia. The subjects clinically affected were almost always collaterals (usually 2 brothers), whose parents were free from the disease. This fact strongly supports the view that the transmission of the disease is recessive. Hemochromatosis occurs more often in men than in women, probably as a result of sex-limitation—a phenomenon which is phenotypical and not genotypical. Its lower incidence in women can presumably be explained by the occurrence of menstruation, pregnancy, and lactation, which tend to prevent the accumulation of iron reserves in women. Proof of direct transmission of the disease was obtained, for the first time, by the authors when they demonstrated the existence of subclinical hemochromatosis in the daughter of a woman with proved complete hemochromatosis.

In an addendum, the authors discuss the views expressed by Cachin and co-workers in an article published (*Semaine hôp. Paris* 33:3174, 1957) after their own paper was written. They believe their findings controvert Cachin's suggestion that hemochromatosis can be divided into 2 distinct conditions: (1) idiopathic hemochromatosis, in which alcoholism plays no part, and (2) alcoholic hemochromatosis, in which heredity has no significance.

Hereditary Capillary Purpura (von Willebrand's Disease). A. R. Horler and L. J. Witts. Quart. J. Med. 27:173-185 (April) 1958 [Oxford, England].

Until the beginning of this century all hereditary hemorrhagic disorders were regarded as hemophilia, irrespective of their clinical or genetic characteristics. Osler established hereditary hemorrhagic telangiectasia as a separate entity in 1901, and some years later, with the publication in 1913 of a paper by Austin and Pepper, it became apparent that there was a third variety of hereditary hemorrhagic disorder which bore a closer resemblance to the purpuras than to hemophilia. There followed the report by Glanzmann in 1918 of a hemorrhagic state which he ascribed to a functional abnormality of the blood platelets, and to which he

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The place of publication of the periodicals appears in brackets preceding each abstract.

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gave the name of "hereditary hemorrhagic thrombasthenia." Von Willebrand in 1931 reported having studied a family of bleeders in the Aaland Islands. Twenty-three members of a family of 66 complained of hemorrhagic symptoms, consisting of bleeding on trivial injury or spontaneous bleeding from the nose, gums, skin, genitals, or gastrointestinal or urinary tracts. The platelet counts were normal, as was the platelet morphology, but the bleeding time was greatly prolonged and the tourniquet test positive; coagulation time and clot retraction were normal. Von Willebrand at first named the condition "hereditary pseudohemophilia," a name which has since been applied to other hemorrhagic diseases. As a result of experiments intended to show the inability of the platelets to occlude a glass capillary tube, he renamed the condition "constitutional thrombopathy." The authors describe the clinical features of this condition and discuss its classification in the light of the tests which are now available for the investigation of hemostasis.

In the experience of the authors, hereditary capillary purpura is the second commonest hereditary hemorrhagic disorder. In a series of 80 cases of hereditary hemorrhagic disorders seen in Oxford, 52 were examples of hemophilia or Christmas disease, 19 of hereditary capillary purpura, 7 of hereditary hemorrhagic telangiectasia, 1 of congenital afibrinogenemia, and 1 of a dual hemostatic defect. Thus hereditary capillary purpura (von Willebrand's disease) accounts for about one-quarter of all cases of hereditary hemorrhagic disease. It is associated with an abnormality in the structure and function of the capillaries, which results in a prolonged bleeding time. Much less frequently in hereditary purpura a disturbance in the functional efficiency of the platelets can be demonstrated, when the condition may be referred to as hereditary thrombocytopathic purpura or Glanzmann's disease. There are also cases of hereditary thrombocytopenic purpura. In rare cases hereditary capillary purpura may be combined with a deficiency of one of the clotting factors, notably antihemophilic globulin. The terms "thrombasthenia" and "pseudohemophilia" are ill-defined and should be avoided in classifying the hereditary hemorrhagic diseases.

Hereditary Hemorrhagic Telangiectasia (Osler): Two Cases with Examination of Family. E. Mortensen. Ugesk. læger 120:575-576 (April 24) 1958 (In Danish) [Copenhagen].

Hereditary hemorrhagic telangiectasia, or Osler's disease, is one of the most uncommon causes of hemorrhagic diathesis and has previously been described in only 7 cases in Denmark. It is a vascular anomaly seen clinically as a hemorrhagic diathesis without demonstrable cause on the usual laboratory examinations and is pathoanatomically characterized by multiple telangiectases in skin and mucous membranes. The hemorrhages usually appear as epistaxes but follow the extent of the telangiectases and not infrequently occur in the mucous membranes of the digestive canal and urogenital organs and have been described in retina and cerebrum. The picture is marked by recurrent bleeding and resulting anemia. The anemia is of simple hemorrhagic type and often grave. The angiectases vary from the size of a pinhead to the size of a pea. The most frequent visible localizations are the skin of the face, lips, mucous membranes of tongue and oral cavity, conjunctiva, and skin of fingers and toes. Treatment is limited to hemostasis, where this is possible, and correction of the anemia by administration of iron. No causal therapy is known. There is simple dominant inheritance. In the homozygote form of the disease, described in one instance, the patient died at the age of 11 weeks. In the heterozygote form the prognosis is always good. The 2 cases reported were in relatives, a girl, aged 10 years, and a woman, aged 43. Investigations revealed epistaxis in 14 out of 21 members of 2 generations of the family.

Idiopathic Myocardial Hypertrophy. D. H. Spodick and D. Littmann. Am. J. Cardiol. 1:610-623 (May) 1958 [New York].

Idiopathic myocardial hypertrophy is a curious disturbance of the heart which, since its original description in 1901, has remained largely unexplained. One important reason for the imperfect understanding of this disorder has been its comparative rarity and the paucity of well-studied examples. The authors summarize the data on 8 patients with idiopathic myocardial hypertrophy observed at the Veterans Administration Hospital, West Roxbury, Mass., from 1947 to 1956. Two case histories illustrate the problems encountered in this disease. A search of the world literature disclosed 72 reports of patients with the isolated finding of unexplained large heart. Idiopathic myocardial hypertrophy is characterized by cardiac enlargement and progressive decompensation occurring in previously healthy individuals. The sole pathological finding is left ventricular hypertrophy with or without varying degrees of mural fibrosis. Valvular lesions are absent. The coronary arteries are widely patent, and atheromas are either absent or insignificant.

The disease involves mainly young adults. The course of the disorder is unusually rapid in most instances. Embolism is frequent and is related to the common autopsy finding of mural and endocardial thrombi. No clinical or laboratory finding is of specific aid in the diagnosis. Close simulation of specific lesions occasionally leads to mistaken diagnoses, such as arteriosclerotic heart disease, mitral stenosis, etc. The etiology of idiopathic myocardial hypertrophy remains obscure. It may represent one or more processes undetected by present techniques. Various studies are cited which would invalidate the hypotheses of preexisting hypertension, myocarditis, or dietary deficiency as causative factors. This condition should be considered in the differential diagnosis of congestive heart failure of unexplained origin.

Quinidine Therapy for Atrial Fibrillation: Indications and Toxic Effects. S. R. Robbin and E. S. Cohen. Am. J. Cardiol. 1:629-636 (May) 1958 [New York].

Although quinidine has been considered as the chief drug for the suppression of cardiac arrhythmias, there has been a controversy as to whether the benefit from abolishing chronic cardiac arrhythmias and restoring normal sinus rhythm outweighs the risk of its toxic effects on the myocardium and respiratory center, and even of sudden death. The reason why quinidine fell into disrepute shortly after its introduction was due to the limited knowledge of its pharmacological properties. The purpose of this report is to present an unusual case of atrial fibrillation in which digitalis failed to control the ventricular rate, although there was no evidence of acute rheumatic activity, thyrotoxicosis, multiple pulmonary embolism, or Wolff-Parkinson-White syndrome. A situation arose where uncontrolled atrial fibrillation with a very rapid ventricular response caused intractable congestive heart failure with signs and symptoms of a shock-like state. In this desperate situation treatment with quinidine and conversion of atrial fibrillation to a normal sinus rhythm was lifesaving. However, this was complicated by marked sensitivity to quinidine with manifestations of severe quinidine toxicity. The authors stress the importance of frequent electrocardiograms as a guide to the dosage during quinidine therapy and reemphasize the fact that the increase in cardiac output obtained by conversion of atrial fibrillation to normal sinus rhythm may be lifesaving in patients with intractable congestive failure.

Radioiodine Treatment of Paroxysmal Supraventricular Tachycardia in the Euthyroid Patient. E. Corday, H. Gold and H. L. Jaffe. *Circulation* 17:900-906 (May) 1958 [New York].

Twenty-five euthyroid patients with recurrent paroxysmal supraventricular tachycardia, which was resistant to prophylactic treatment with quinidine and procainamide (Pronestyl) hydrochloride, were treated with radioactive iodine (I^{131}). Twenty-two of these patients had arteriosclerotic heart disease, and 3 had rheumatic heart disease. Doses of 6 mc. of I^{131} were given orally at weekly intervals until the patient had received a total dose of 25 to 30 mc. It usually took 2 to 3 months after treatment for the radioactive iodine to reach maximum hypometabolic levels. Twenty of the 25 patients obtained good results with no recurrences, or very few paroxysms, of tachycardia after the period of treatment. In 3 patients the results were considered fair; there were no, or very few, paroxysms for 12 months after the period of treatment, and after that time there were occasional recurrences. The treatment failed in the remaining 2 patients, both of whom were psychotic.

The production of a relative degree of hypothyroidism appears to be necessary in order to abolish attacks of supraventricular tachycardia in previously euthyroid patients resistant to other forms of treatment. The mechanism by which such attacks are prevented by suppressing thyroid function is not clear and requires further studies. Myxedema occurred in 4 of the 25 patients after I^{131} therapy. This was corrected by the administration of thyroid in doses varying from 6 to 45 mg. per day. All the patients were comfortable and had few or no complaints as a result of the reduced thyroid function. It seems clear that the administration of I^{131} is a simple, convenient, and relatively safe method for producing hypothyroidism and preventing supraventricular cardiac arrhythmias.

Staphylococcal Pneumonia: A Review of 21 Cases in Adults. A. M. Fisher, R. W. Trever, J. A. Curtin and others. New England J. Med. 258:919-928 (May 8) 1958 [Boston].

During the period from 1942 through 1956 staphylococcic pneumonia was observed at the Johns Hopkins Hospital in 18 adults. The increasing incidence of this type of pneumonia is demonstrated by the fact that only 4 of the cases occurred during the first 8 years, and the other 14 in the remaining 7 years of the period. Three patients with staphylococcic pneumonia observed during the last 3 years at another hospital are added, making a total of 21 cases analyzed. The clinical courses of 5 of these patients presented features of unusual interest and are described in detail. Fourteen of the total group were males, and 7 were females. The age range was 15 to 81, with an average of 52 years. Fourteen of the patients died—a mortality of 67%. In 14 of the patients the infection apparently had its origin in the lungs, but in 7 there was a staphylococcic infection elsewhere that may have served as the focus from which the infection spread to the lungs. In 3 patients the skin was apparently the portal of entry; other conditions responsible for secondary cases were a peritonsillar abscess, a bronchopleural fistula, and a septic abortion. In the last patient the pulmonary findings dominated the clinical picture. Eight patients had had antecedent antibiotic therapy, and 2 received corticosteroids in addition. The antibiotics employed were penicillin, streptomycin, and the tetracyclines, used as nonspecific "prophylactic" measures in 5 patients and instituted for the treatment of a known infection in the other 3. Six of these 8 patients died. Eighteen patients received some type of antibiotic therapy for the staphylococcic infection; 16 were given penicillin, which was combined with other antibiotics in 12 cases. The recovery rate in this group was 7 out of 16.

Eleven of the 14 patients who died had serious debilitating diseases that played a predominant part in the outcome, although all deaths were directly due to the staphylococcic infection. Two patients had fulminating pneumonia, leading to death within 3 days. In 2 cases the clinical picture suggested that the staphylococcic pneumonia occurred secondary to influenza, but there was no other evidence to substantiate that diagnosis. The cases of staphylococcic pneumonia appeared as isolated ones at times when no outbreaks of influenza had been recognized. However, when cases of staphylococcic pneumonia are encountered, concomitant influenza should be suspected.

The authors conclude that infections due to drug-resistant staphylococci represent the most serious hazard. There is no evidence that "prophylactic" antibiotic therapy is of any value, and there is at least suggestive evidence that the employment of antibiotics in this fashion may be deleterious. The fulminating staphylococcic infections provide the most serious challenge. The characteristics of such a rapidly fatal state suggest that elaboration of 1 or more bacterial toxins may be responsible for the severe prostration and rapid termination. The increased prevalence of staphylococcic pneumonia in adults can be partly accounted for by infections that occur in patients after admission for some unrelated serious malady.

Amelioration of Diabetes Mellitus by an Insulinoma. R. D. Gittler, G. Zucker, R. Eisinger and N. Stoller. New England J. Med. 258:932-935 (May 8) 1958 [Boston].

The occurrence of a functioning islet-cell tumor of the pancreas in a patient with diabetes mellitus is an exceedingly rare phenomenon. The authors recently observed a patient who experienced a gradual amelioration of diabetes over a period of 9 years, which finally culminated in frank episodes of spontaneous hypoglycemia. Laparotomy revealed a large islet-cell tumor of the pancreas. Excision of the neoplasm afforded complete relief of the hypoglycemia and reemergence of the diabetic state. The preoperative diagnosis of an insulinoma was complicated by coexistence of diffuse liver disease. The patient died 24 days after the operation from a massive intra-abdominal hemorrhage. Postmorten study showed the immediate cause of death to have been erosion of a ligature surrounding a splenic vessel. The remaining pancreatic tissue was normal. The liver was cirrhotic.

Response of Serum Lipids and Lipoproteins of Man to Beta-Sitosterol and Safflower Oil: A Long-Term Study. J. W. Farquhar and M. Sokolow. Circulation 17:890-899 (May) 1958 [New York].

A 7-phase study of the comparative effects on serum lipid levels of the single and the combined administration of plant sterols (beta-sitosterol) and a highly unsaturated vegetable oil (safflower oil) was carried out for 35 to 54 weeks in 15 ambulatory nondiabetic persons, between the ages of 36 and 63 years. There were 14 men and 1 woman, 13 of whom had either arteriosclerotic heart disease or arteriosclerosis obliterans, 1 had no apparent disease, and 1 had mild hypertension. The study was divided into 4 control periods (phases 1, 3, 5, and 7), of about 6 weeks each, alternated with 3 test periods (phases 2, 4, and 6), averaging 8 weeks in duration. The persons studied were given in random sequence 18 Gm. of beta-sitosterol per day in conjunction with the control diet which contained 39% of calories derived from animal or hydrogenated vegetable fat; 81 Gm. of safflower oil per day as 31% of total calories in equicaloric substitution for animal and hydrogenated vegetable fat of the control diet; and a combination of the 2. Placebos were administered during the control period that preceded and followed each test period. The serum lipid levels were determined weekly.

A rapid and sustained fall in beta-lipoprotein cholesterol (BLPC) level, total lipid level, and phospholipid level occurred during each of the 3 test periods. The average fall in BLPC level after ingestion of the test agents was as follows: after ingestion of sitosterol alone, 22%; after ingestion of safflower oil alone, 22%; after ingestion of the 2 combined, 34%. Average body weights were constant during the study, and the average serum cholesterol concentrations were closely similar during the 4 control periods. The uniformity of the response of the serum lipid level to the test agents, coupled with the stability of average body weights and control BLPC concentrations, indicates that confidence can be placed in the results of long-term dietary studies in which nonformula diets are used in well-instructed ambulatory patients.

The fall and subsequent rise in the BLPC level were more rapid with sitosterol than with safflower oil, suggesting that the 2 agents have different mechanisms of action. The 55% greater fall in the BLPC level after ingestion of sitosterol and safflower oil combined indicates that the action of safflower oil is not likely to be the result of the small amount of sitosterol it contains. Investigation of the effects of ingestion of pure fatty acids to which varying amounts of sitosterol can be added might aid in clarifying the role of sitosterol in the action of vegetable oils. Since no significant changes in the alpha-lipoprotein cholesterol and triglyceride concentrations were observed during the study, it was concluded that the S_f 0-10 fraction of the serum beta-lipoproteins was primarily affected by the test agents.

Bornholm Disease in an Adelaide Suburban Area. L. Kaupmees and R. A. A. Pellew. M. J. Australia 1:517-518 (April 19) 1958 [Sydney].

Kaupmees and Pellew describe an outbreak of Bornholm disease in a suburb of Adelaide. This disease is also known as epidemic pleurodynia or as epidemic myalgia. Twenty-three patients with this disorder were observed in a new housing area. All the patients lived in homes surrounding 2 shopping areas. The outbreak was definitely localized, as no cases occurred in the zone immediately surrounding the area. Intense headache, usually of a bursting nature, and occipital or frontal or both, was one of the outstanding symptoms. Other symptoms were low-grade fever, stiffness in the back of the neck, and muscle pain along the attachment of the diaphragm, the upper part of the trapezius, and, peculiarly, a triangle area in the quadriceps femoris in the front of the thigh. All the patients complained of pain in the orbit when the eyes were moved from side to side. Nausea, vomiting, and constipation were common, and vertigo occurred in every case. There were no physical signs of note, except tenderness under both costal margins and neck stiffness. A pleural friction rub was not discovered in any case.

Treatment consisted of bed rest and symptomatic measures. The patients obtained great relief from the unpleasant vertigo when given Dramamine derivatives, often combined with pyridoxine. The tranquilizing drugs relieved the depression. The treatment of the patients with short-lived illness was simple, but those with sustained pyrexia presented a greater problem. Intravenous injections of arsenic were tried with good effect in 1 patient, but the disease process may well have burned itself out without the use of arsenic. Ten patients were observed later, and no residual muscle weakness was detected.

Epidemiological and Laboratory Investigations on Bornholm Disease in Adelaide, 1957. A. E. Duxbury and P. Warner. M. J. Australia 1:518-523 (April 19) 1958 [Sydney].

This report is concerned with certain epidemiologic observations made on the patients whom Kaupmees and Pellew described in the preceding paper, but since it has been shown that certain members of the Coxsackie viruses, group B, are associated with Bornholm disease and with a proportion of cases of aseptic or benign meningitis, Duxbury and Warner traced 30 additional cases of epidemic myalgia and 2 of benign meningitis which were attributed to a Coxsackie virus. The first point of epidemiologic interest that arose from the investigations was that Bornholm disease was not confined to the circumscribed area described by Kaupmees and Pellew, but that cases occurred in most geographical sections of metropolitan Adelaide, although there may have been a concentration of patients in a new housing area. There was a preponderance of women, and most of the patients were aged from 20 to 54 years. The outbreak was spread out over the whole year.

A Coxsackie virus, group B, type 2, was isolated from 1 patient, in whose serum a rising titer of antibodies against the virus was demonstrated. This established for the first time an association between Coxsackie B-2 virus and Bornholm disease. Two viruses isolated from the patients with aseptic meningitis were almost certainly identified with the B-2 strain obtained from the patient with Bornholm disease. Among the serums of 24 patients with Bornholm disease, 13 had neutralizing activity against the isolated virus. Except in serum from the above-mentioned patient, no rising titers of antibodies could be demonstrated. In addition to the successful isolations, unsuccessful attempts were made to isolate viruses from 21 patients and 8 family contacts of patients. The failure to isolate viruses and to demonstrate rising antibody titers is discussed, and it is thought that, in spite of this, it is possible that the whole outbreak may be attributed to the Coxsackie B-2 virus.

Some Remarks on Prognosis of Tetanus. H. Imdahl and U. Gött. Arch. klin. Chir. 288:162-170 (No. 2) 1958 (In German) [Berlin].

The authors report on 43 patients with tetanus who were admitted to the surgical clinic in Bonn, Germany, during the last 30 years; of these, 29 died. The observations made on these patients convinced the authors that 3 types of the course of the disease must be distinguished. Patients with the mild type show only locally limited manifestations (trismus, opisthotonos, risus sardonicus, and local muscle rigidity). Patients with the moderately severe type show, in addition, single, not generalized, bouts of spasms or occasionally 1 generalized bout. Patients with the severe type show frequent generalized spasms in addition to the manifestations observed in patients with the other 2 types. From a consideration of these 3 types it appears that the length of the incubation period has no prognostic value, because neither the incubation period nor the initial symptoms of tetanus provide any information concerning the future course of the disease. The time which elapses between the first manifestation of the disease and the first occurrence of spasms is called the "invasion period." The cure rate was found to be 33% among the patients with an invasion period of more than 4 days, in contrast to a cure rate of only 9% among those with an invasion period of less than 4 days. Invasion periods of more than 4 days in length were observed in 4 patients with the moderately severe or the severe type of the course of the disease, in whom immediate combined administration of high doses of tetanus antitoxin and penicillin was practiced. Since the length of the invasion period apparently can be influenced therapeutically, it seems to have more prognostic value than the incubation period. Immediate treatment is essential for all patients, not just for those with stormy initial manifestations. The prognosis is the more favorable the earlier high doses of tetanus antitoxin and antibiotics are given. The technique and the evaluation of the so-called preliminary tests, i. e., the intracutaneous test and the ophthalmic reaction, are practicable and make it possible largely to exclude the occurrence of primary anaphylactic shock. The patients should be admitted to a hospital which offers the adequate staff and apparatus for the most modern methods of treatment.

A Clinical Test for Esophagitis. L. M. Bernstein and L. A. Baker. Gastroenterology 34:760-781 (May) 1958 [Baltimore].

A controlled test was designed to elicit the symptoms of esophagitis by continuous perfusion of the esophagus with 0.1 *N* hydrochloric acid. Criteria were established to differentiate esophageal from gastroduodenal origins of experimentally induced symptoms. Fifty-five subjects were studied. Results of the tests were related to esophagoscopic findings in 43 patients. A test with positive results elicited typical clinical symptoms in 9 of 10 patients with endoscopically demonstrable esophagitis, in 10 of 12 patients with psuedoesophagitis (esophagitis by clinical history but without endoscopic abnormality), and in 3 of 4 patients with esophagitis by history who were not examined esophagoscopically. A negative test (failure of acid perfusion to elicit symptoms) was found in 20 of 21 patients with neither history nor endoscopic findings of esophagitis, and in all 8 patients without history of esophagitis who were not examined endoscopically. The test confirmed the esophageal origin of symptoms in patients with endoscopic evidence of esophagitis. It objectively demonstrated the esophageal origin of symptoms arising in the esophagus with normal endoscopic appearance and with normal roentgenologic findings. The test effectively differentiated esophageal from cardiac pain.

The harmlessness of the test was demonstrated by (1) its failure to elicit symptoms in normal subjects, (2) the lack of esophagoscopic abnormality induced by the test, (3) the absence of either electrocardiographic changes or cardiac pain in patients with coronary artery disease with or without angina, and (4) the lack of recurrence of gastrointestinal bleeding in patients with recent gross bleeding episodes. The high degree of success of this test in eliciting the symptoms of esophagitis, as compared with the ineffective or inconsistent results of previous investigators, must be attributed to both the longer duration of perfusion and the greater quantity of acid used.

Cytology in the Diagnosis of Gastric Cancer: The Significance of Location and Pathologic Type. W. O. Umiker, R. J. Bolt, A. D. Hoerzema and H. M. Pollard. Gastroenterology 34:859-866 (May) 1958 [Baltimore].

The authors undertook this study to determine the significance, if any, of location and pathological type of gastric cancer in cytological diagnosis. The accuracy of cytological diagnosis of 38 gastric cancers by a chymotrypsin lavage technique was 89.5% (65.8% positive, 23.7% suspicious). Negative smears were found in 92.3% of 78 patients who did not have cancer of the stomach. There were 2 false-positive reports. Ten of 17 cancers in the distal portion of the stomach were detected cytologically. These 17 patients included 6 who had unsatisfactory specimens. The best results were obtained from patients with neoplasms which were located at the cardia or which involved a major portion of the stomach. Equivocal smears were found most frequently in ulcerating cancers, probably because of a barrier of necrotic cells. Polypoid and diffusely infiltrating neoplasms were detected with greater accuracy. Positive smears were found in 17 of 20 patients with adenocarcinoma (85%), in 1 of 7 patients with anaplastic carcinoma (14%), and in 2 of 4 patients with lymphoblastoma (50%). The lower accuracy in the group of patients with anaplastic carcinoma was probably the result of failure to recognize the less conspicuous undifferentiated cells. There were no false-negative results in the group of patients with scirrhous carcinoma, but 19% of the medullary carcinomas were missed cytologically because of greater anaplasia, necrosis, and secondary inflammation. Additional cytological specimens should be examined when the initial smears give equivocal or negative results.

SURGERY

Aortic Stenosis. P. Wood. Am. J. Cardiol. 1:553-571 (May) 1958 [New York].

Observations on aortic stenosis were obtained by analyzing a consecutive series of 250 patients who were under the author's personal observation during the last 7 years. Patients with dominant mitral valve disease were excluded. The available methods for surgical repair of severe aortic stenosis, particularly of the acquired type, are far from ideal. The author regards valvotomy by the Brock technique as the most feasible at the present time. He describes the important physical signs and the electrocardiographic and x-ray findings, the changes in the direct brachial arteriogram and central aortic pressure pulse in the various grades of aortic stenosis, and the modifications which occur when it is combined with aortic incompetence and mitral valve disease.

The indications and contraindications for aortic valvotomy are discussed on the basis of these findings and of the results of valvotomy in 80 patients. The results obtained in these 80 patients are compared with those obtained in 64 patients treated medically. In the surgically treated patients the immediate and remote mortality was 20%, whereas in the medically treated patients it was well over 30%. Good results were obtained in 54% of those subjected to surgery, an achievement quite impossible by medical means. The author concludes that patients with serious aortic stenosis who have symptoms should be offered surgical treatment. However, valvotomy is still too hazardous to advise when it is most desirable (asymptomatic patients) and too late when surgery appears imperative (patients with heart failure); nevertheless, the results of skilled surgical treatment far outweigh anything that medical treatment has to offer.

Results in the Surgical Treatment of Mitral Stenosis. W. L. Diveley, R. A. Daniel Jr., H. W. Scott Jr. and J. H. Foster. Ann. Surg. 47:614-624 (May) 1958 [Philadelphia].

The ideal objective of mitral commissurotomy is the complete opening of the fused valve and mechanical separation of any fusion of the chordopapillary system without producing mitral insufficiency. With pump-oxygenators being available and the increased success of techniques of intracardiac surgery under direct vision, the question arises concerning the advisability of using these techniques in the correction of mitral stenosis. This report reviews the results which have been obtained by nonvisual methods of surgical treatment in mitral stenosis at the Vanderbilt University Hospital with the hope of formulating a rational approach to the question of "open" surgery in this disease. One hundred forty-eight patients were subjected to operation for mitral stenosis. The records of clinical evaluation were available on 108 patients, all of whom were found at operation to have stenosis. Varying degrees of insufficiency were also present in 40 patients. Twelve patients died of complications associated with the operation, a hospital mortality rate of 11%. Seven late deaths occurred, 2 from accidental causes in patients who had obtained excellent clinical improvement. Twenty patients, including those classed as late deaths, either were unimproved or were worse after the operation. The causes of failure in the majority of these appeared to be associated insufficiency of the valve or incomplete separation of the valve leaflets at the time of operation.

Other factors which prevented improvement and which contributed to the death of some patients were: (1) the presence of chronic auricular fibrillation; (2) the presence of calcification of the valve leaflets or of intra-atrial thrombosis; (3) the presence of advanced pulmonary and myocardial damage associated with mitral stenosis of long standing. Definite, and often marked, improvement of the patients' physical status was achieved in 76, or 70%, of the group. It would appear that the opportunity for further advancement in the treatment of acquired valvular disease lies in the utilization of techniques which allow for the direct visual repair of defects and ultimately, perhaps, for the replacement of those valves which are irreparably damaged by suitable prosthetic devices.

Hydatid Cysts of the Heart (With Reference to Two Cases). R. de Vernejoul, R. Poinso, A. Jouve and others. Presse méd. 66:697-700 (April 23) 1958 (In French) [Paris].

The authors report on 2 patients, a 30-year-old man and a 31-year-old woman, with hydatid cysts of the heart, both of whom were cured by surgery. The onset in the first patient was characterized by transient attacks of fainting, pain in the chest on the left side, and fever. Roentgenograms made 7 years earlier had revealed enlargement of the heart. The patient's general condition on admission to hospital was good. Laboratory findings, apart from a slight eosinophilia, were negative. Radiographic studies showed a juxtacardiac opacity on the left side and in front of the heart. The significant association which was found between the angiographic pictures and the electrocardiagraphic tracings led to the diagnosis of a voluminous tumor, either of the myocardium or of the epicardium on the left side of the heart. At operation a cyst the size of a large orange, with multiple irregularities, localized at the level of the lateral wall of the left ventricle, was found and excised. The patient's postoperative course was uneventful, and he was able to return to work. Three months later both his general condition and the roentgenoscopic outlines of the heart were excellent.

The case of the second patient is interesting because of the rarity with which hydatid cysts of the the heart occur in women. Her history, which was highly significant, revealed an appendectomy, performed several years before, in the course of which a hydatid cyst was detected in the appendicular region. Three years later she was operated on because of violent abdominal pains, and a peritoneal echinococcus was found. One year later the patient was operated on again, and the primary hydatid cyst in the liver, which must have been responsible for the infestation of the iliac cavity on the right side detected at the first operation, was removed. Five years later she was hospitalized for a severe cardiovascular collapse, associated with diarrhea, vomiting, and fever. Blood studies showed significant eosinophilia. Roentgenologic examination revealed slight enlargement of the left ventricle of the heart, and the electrocardiographic tracings showed coronary ischemia. Angiography revealed a sinuous biconcave downward curve (Canabal's rounded lacuna), considered typical by South American authors. At operation a large cyst, the size of an orange, containing multiple daughter cysts, was found in the left ventricle and removed. The postoperative course of the patient was uneventful, and several weeks later her heart had decreased distinctly in size.

The authors emphasize the following points: (1) the fact that the cysts occur most frequently in the left ventricle, (2) the latency of the clinical symptoms, and (3) the diagnostic value of angiocardiography in conjunction with electrocardiography. Surgery at the present time is the only effective treatment for hydatid cysts of the heart, and gives excellent results in the more common forms of the disease. Less common forms involving localization of the cyst in the atrium or the septum or still graver eventualities, such as intracavitary rupture, pose more delicate problems which may perhaps belong to the domain of open heart operations.

Resection for Pulmonary Tuberculosis: A Four-Year Follow-up Study. D. B. Hiscoe, W. F. Thompson, T. J. Enright and H. Black. New England J. Med. 258:863-869 (May 1) 1958 [Boston].

The authors report on 80 patients, most of them young men, with pulmonary tuberculosis, who underwent unilateral pulmonary resection at a Veterans Administration hospital between 1949 and 1953 and were followed postoperatively for 4 years or more. Sixty-two (77%) of the 80 patients had a positive sputum, either by culture or by smear, within 3 months before operation. Fifty-two patients (65%) had received collapse therapy before resection, and 18 of these had undergone thoracoplasties; 16 of the latter underwent resection because of failure of thoracoplasty. Forty-two patients (51%) had bilateral disease. Eighteen patients (23%) underwent resection for what was considered to be relatively unstable cavitary disease. Lobectomy alone or combined with segmental resection was performed on 65 patients, pneumonectomy on 5, segmental resection alone on 6, and wedge resection on 4. Forty-five of the 80 resections were followed by thoracoplasties, 23 of which were done to prevent overexpansion of the remaining lung and not for specific complications. Chemotherapy, consisting for the most part of combined administration of streptomycin and aminosalicylic acid, was used erratically, some patients receiving long and others short courses. Most patients were given more chemotherapy postoperatively than preoperatively.

Despite unfavorable factors for elective resection, such as positive sputum, unstable cavitary disease, failure of preceding thoracoplasty, and presence of bilateral disease in a large number of patients, results were satisfactory. Fifty-eight (72%) of the 80 patients are now well and able to work and have had stable roentgenographic findings since the operation; 41 of the 58 patients also had negative sputums since the operation, and all but 3 of the remaining 17 patients had a positive sputum only once or twice postoperatively. Ten patients (13%) are currently well and on full physical activity but have required definitive treatment for tuberculosis since the resection. Four patients (5%) are currently ill because of persistence of disease or its complications. Eight patients (10%) died. Most of the poor results were evident within 18 months after the resection. The poor results were heavily concentrated in the group of 62 patients who had a positive sputum at the time of surgical intervention. Eleven patients (14%) had postoperative tuberculous complications (bronchopleural fistula, empyema, or spread of disease), and all of them belonged to the group of open-positive cases. Only 3 of the 11 patients obtained a satisfactory result. When the various chemotherapeutic regimens were compared, it appeared that those who received more than 30 days of preoperative chemotherapy had a slightly larger number of satisfactory results. Eighty-three per cent of those who received more than 180 days of total (preoperative and postoperative) chemotherapy had satisfactory results as compared with 66% of those who received less than 180 days of total chemotherapy. Twelve (55%) of the 22 patients with unsatisfactory results had received no chemotherapy or only insignificant amounts. Postoperative thoracoplasty did not appear to alter results favorably unless done for a specific complication. The factors that were correlated with a good long-term result were as follows: unilateral disease; stable residual lesion; negative sputum preoperatively; preoperative chemotherapy for 30 days or more; total chemotherapy for 180 days or more; and prompt conversion to negativity postoperatively.

Dissecting Aneurysm of the Aorta: A New Surgical Problem. R. P. McGurney and T. S. Rodda. Am. Surgeon 24:381-384 (May) 1958 [Baltimore].

The authors report on 10 men and 3 women with dissecting aneurysm of the aorta who died at several hospitals in Memphis, Tenn., and on whom autopsies were performed. Of these, 3 were in the

4th decade, 7 in the 5th decade, 2 in the 6th decade, and 1 in the 7th decade. Ten of the patients had significant histories of hypertension, 1 had previously had a myocardial infarction, 1 had a history of angina pectoris, and 3 had preceding renal disease. Twelve of the 13 patients had outstanding complaints of acute pain: the pain was felt in the chest and upper back in 7 in whom the thoracic aorta was the original site of dissection; in 3, the pain began in the epigastrium and radiated into the flanks; and in 2 others, the pain was first noticed in the lower abdomen and progressed to the lower extremities which had evidence of arterial occlusion. Two patients had neurological symptoms, manifested by a brief period of stupor and semiconsciousness in 1 and a brief convulsion in the other. Two patients had severe headache, and 2 others had dyspnea. On admission to hospital, 4 patients had signs of shock; 5, apical systolic murmurs; 3, pulmonary rales; 3, abdominal tenderness; and 2, absent pulses in the lower extremities. The time interval between the onset of a significant disturbance and death varied from 12 hours to more than 1 week. The primary cause of death in all the patients was dissecting aneurysm, with cardiac tamponade in 3, hemorrhage and shock in 9, and apparently congestive failure in 1.

Of prime importance to one who would recognize and surgically treat dissecting aneurysm is the gross appearance of the lesion. This was described as hemorrhagic and markedly distended in 5 patients; the aorta measured 8 cm. in diameter in 1 patient. In those in whom rupture had occurred, a large blood clot was present in the aortic area. In 6 patients the extent of aortic dissection was from the aortic valve to the aortic bifurcation; in 4 the dissection involved the arch of the aorta from the valve to the upper thoracic aorta; and in 3 patients it primarily extended from the left subclavian area to the aortic bifurcation. An intimal split was noted just above the aortic valve or in the arch area in 10 patients, and just distal to the left subclavian artery in the remaining 3. Rupture of the aorta occurred in 9 patients. Microscopic examination revealed evidence of so-called idiopathic medionecrosis in 12 of the 13 patients. Significant associated pathological lesions consisted of arteriosclerosis in coronary and other vessels in 8 patients, pulmonary tuberculosis in 1, pulmonary infarction in 1, and cardiac enlargement with hypertrophy in 11.

From the small number of patients with dissecting aneurysm of the aorta who underwent surgical treatment and whose cases were collected from the literature, one can readily discern that this method of treatment is not only a new one but one which has not been fully developed. Yet the successes already achieved indicate that it is a tremendous improvement over the watch-and-wait-and-hope methods which result in death in 90% of such patients. With the advent of successful surgical treatment, it behooves both surgeon and internist to improve their diagnostic discrimination in regard to this condition. One should consider dissecting aneurysm in any patient with severe chest, back, or abdominal pain. Methodical study with proper use of laboratory aids should enable one to make the correct diagnosis in 80 to 90% of the patients. Dissecting aneurysm is a surgical emergency, and the thoracic surgeon should lose no time in carrying out treatment.

Surgical Correction of Atrial Septal Defects Under Control of Vision, by Use of a New Artificial Heart-Lung Apparatus: Results in Six Cases. H. J. Felipozzi, L. Gomes D'Oliveira, S. Paladino and others. Rev. paulista med. 52:157-168 (March) 1958 (In Portuguese) [São Paulo, Brazil].

Congenital atrial septal defects require early surgical correction before the appearance of symptoms indicating stasis in pulmonary circulation and overloading of the right side of the heart. Surgical closure of the septal gap must be made under direct visual control in an empty heart. American and European cardiologists in specialized hospitals use the artificial heart-lung machine as a temporary substitute for cardiopulmonary functions during intracardial surgery on an empty heart. The authors describe a new artificial heart-lung machine which permits extracorporeal circulation with a physiological output. The apparatus is depicted in illustrations, and its functioning is shown by means of a schematic drawing. It consists of (1) an oxygenator of the rotating disk type, (2) a pump of the De Bakey type for propulsion of oxygenated blood in a continuous flow, and (3) a system for reutilizing intracardiac blood, consisting of a pump for aspiration of blood from the venous sinus and its reunion with the systemic circulation through the oxygenator. The new heart-lung machine described by the authors was used for the correction of atrial septal defect in 6 patients, between the ages of 13 and 18 years. Complete correction of the septal defect under direct visual control of the gap was obtained. The apparatus devised by the authors has the following advantages: 1. It permits the use of a physiological, individual flow per minute. This is obtained by letting all the caval blood flow by gravity, instead of calculating previously the amount of blood which should be sent to the systemic circulation. 2. The oxygenator can oxygenate a large blood flow per minute without any trauma to the blood cells or any important metabolic change. 3. The machine can be used as long as necessary to repair the defect; it has been employed in experimental surgery for more than an hour without significant blood or metabolic changes. 4. The new system is a small manageable unit. It may be used to expose the interior of an empty heart for as long as necessary for the correction of the most complicated septal defects, including additional unsuspected defects found at surgery. The authors advise the use of the heart-lung machine for correction of all atrial septal defects. They emphasize the necessity of a well-trained team to carry out the multiple details involved in open heart surgery with the heart-lung machine.

Spontaneous Rupture of the Esophagus. J. W. Pate, F. A. Hughes and T. B. Patton. Am. Surgeon 24: 385-394 (May) 1958 [Baltimore].

The authors report on 7 men, between the ages of 40 and 62 years, with spontaneous rupture of the esophagus, who did not have the benefit of early surgical intervention. The history and the results of the physical examination were atypical, with pain present in only 2 patients, and vomiting related to onset in only 2 patients. Shock was absent in 3 patients and occurred only 8 to 10 hours after onset in 3 other patients. Cyanosis was marked in only 2 patients, in contrast to its presence in 60% of the patients whose cases were collected from the literature. Slight-to-moderate epigastric tenderness was present in all but 1 patient, and dyspnea was present in all. An erroneous diagnosis was made initially in all the patients, and 5 of them died. A conservative approach was used in the 2 surviving patients. Levin tubes were inserted to prevent further contamination; oral intake was stopped, and intravenously administered fluids were given. Broad-spectrum antibiotics were administered, and empyema pockets and suppurative mediastinitis were drained. The patients responded to this type of conservative therapy. However, after an initial improvement, a plateau was reached when closure of the perforation was indicated before any further improvement was likely. A standard posterolateral thoracotomy incision was used for resecting a lower rib. The mediastinal pleura was widely incised and the esophageal defect closed with 2 layers of nonabsorbable suture. Large tubes were placed in the apex and the base of the chest and connected to underwater drainage. The wound was closed with anatomic layers, leaving the mediastinum open. Suppurative pericarditis occurred as a late complication in 1 patient and was treated in the usual manner.

The prognosis of spontaneous rupture of the esophagus is extremely poor. An immediate diagnosis is necessary to save the patient's life. If examination has shown abnormal chest findings, the patient may be given 20 cc. of iodized oil to swallow just before the emergency chest roentgenogram is made. This procedure will usually allow a definite diagnosis. In the patient in whom there is obvious pleural effusion, particularly with respiratory embarrassment, it may be desirable to do a thoracentesis even before a chest roentgenogram is made. In this event, and in those patients who already have intercostal tube drainage, a small amount of methylene blue may be given by mouth and promptly recovered from the chest fluid. Another simple ward test includes testing of the fluid by litmus paper to be sure of its gastric origin. All 3 of these elementary, rapid, and easy procedures should be used, because the defect may sometimes not be visualized on a single exposure with a Lipiodol swallow and the dye may not immediately appear in a long-standing case with loculated empyema pockets, as happened in 1 of the 2 surviving patients. Early and bold surgical treatment can bring the mortality rate down to a respectable level. If the patient has survived several days when he is first seen, surgery is probably best delayed. The good results which may follow a conservative approach are not usually appreciated.

Cystic Duct Remnant: A Cause of Biliary Distress Following Incomplete Cholecystectomy. T. K. I. Larmi and G. Flock. Acta chir. scandinav. 114:361-378 (No. 5) 1958 (In English) [Stockholm].

The authors report on 13 women, between the ages of 19 and 63 years, who had undergone cholecystectomy and in whom acute upper abdominal pain, similar to that experienced before cholecystectomy, was caused by the ingestion of fat-fried food and in some also by eggs, apples, or spices. The pain was aggravated by work in 5 patients and by bending forward in 3. Four patients reported a direct continuation of their preoperative distress. The other patients had a pain-free interval varying from 1 month to 18 years. In addition to this pain, all patients complained of occasional sensations of fulness, frequent nausea, and occasional vomiting and meteorism. Five patients were constipated. Transitory jaundice was present in 6 patients. Peroral cholecystography was performed on 4 patients, but the bile ducts were not visualized in any of these patients. Intravenous cholecystography was performed on 9 patients, and in 6 of these an enlarged cystic duct remnant was visualized. Two radiopaque areas were also seen in 1 of these remnants, which later were found to be stones.

The patients were reoperated on and a cystic duct remnant was found in 11 patients, and remnants consisting of the cystic duct and a small portion of the neck of the gallbladder in 2. In 9 patients, the remnant of the cystic duct had been inserted into the lateral aspect of the bile ducts. The cystic duct remnants were removed by reoperation. After that, 11 patients were asymptomatic, 2 had occasional mild pain and vomiting, and 1 was still in the hospital. Two hundred forty-one cases in which postcholecystectomy distress was ascribed to a cystic duct remnant were collected from the literature. Stones were present in the common bile duct in 25 to 33% of these cases, but they were not observed in any of the 13 patients in this series. Stones were found, however, in the cystic duct remnants of 2 of the 13 patients and in those of 43 patients whose cases were collected from the literature. A cystic duct remnant should be considered 1 of the factors causing distress after cholecystectomy. Surgical removal of the stump is necessary. At cholecystectomy, care should be taken not to leave a cystic duct remnant.

Cushing's Syndrome in an 18-Month-Old Girl. H. Krauss and H. Krainick. German M. Month. 3:107-109 (April) 1958 (In English) [Stuttgart, Germany].

The authors report on an 18-month-old girl with Cushing's syndrome, who was admitted to the department of pediatrics of the University of Freiburg, Germany, because of increasing obesity. Moderately severe virilism was apparent. There was some pubic hair growth, as well as a clitoris, the size of a bean. Hypertrichosis was marked. The 17-ketosteroid level in the urine was 6 to 8 times that of normal and reflected clinical virilism. In contrast to findings in patients with pure Cushing's syndrome, the increase in height, as well as bone and tooth development, was normal and probably due to the catabolic growth-accelerating properties of androgens; malformation of the vertebrae was also lacking. The blood picture was characteristic, with polycythemia, leukocytosis, and lymphopenia. There was no marked eosinopenia, the initial level, before the performance of the corticotropin test, being 250 eosinophils per cubic millimeter. These unusual findings could not be explained. In addition, there was marked hypertension with a blood pressure of 165/115 mm. Hg. The urinary corticoids were increased typically 4-fold to 8-fold. Equally characteristic was the marked lowering of the carbohydrate tolerance as revealed by a glucose tolerance test. Mixed forms of Cushing's syndrome, combined with adrenogenital syndrome, are observed frequently in childhood.

Tomography after retroperitoneal air insufflation showed a round shadow, 3 cm. in diameter, in the region of the right adrenal. After the usual preoperative preparation with corticotropin, cortisone, and desoxycorticosterone, the patient was operated on; after section of the 12th right rib and opening of the perirenal capsule, a smooth-walled tumor, 4 by 3.5 by 3.5 cm., apparently part of the adrenal, was removed. This tumor was completely surrounded by a tough capsule and was found to be an adenoma. The infant survived the operation well. However, there was no postoperative drop in the blood pressure, which remained high for 5 weeks after resection of the tumor and rose to the extreme values of 240/160 mm. Hg on the second postoperative day; eventually it was restored to normal. In the 6th week after the operation bilateral papilledema and definite widening of the suture lines were observed; these changes were not present before the operation. The papilledema resolved within several weeks and the suture lines closed. There was marked loss of weight, and normal body proportions developed; but despite the comparatively rapid disappearance of Cushing's syndrome, there was no immediate change in the adrenogenital syndrome. Not until 21 months after removal of the adrenal tumor, was the growth of pubic hair observed to have disappeared almost entirely; the hypertrophy of the clitoris remained, however.

The patient was followed up to the age of 5½ years. She developed into an entirely healthy child, but the hypertrophy of the clitoris was still present in the absence of pubic hair. The patient is one of the few with Cushing's syndrome in early childhood who have been cured by removal of an adrenal tumor. It has not been possible to explain the marked postoperative increase in the blood pressure and the occurrence of bilateral papilledema and separation of the suture lines. Initial suspicion of concurrent pheochromocytoma was disproved by the benign course, as well as the absence of vasopressor substances in the urine. It is not impossible that accessory adrenal tissue was stimulated at the operation and led to a transient release of glucocorticoids. Cortisone overproduction can lead to the formation of hepatorenal vasopressor substances that may be responsible for the hypertension associated with Cushing's syndrome. The papilledema and separation of the suture lines might be explained by the same hypothesis.

Total Gastrectomy: Mortality and Survival. O. A. Fly Jr., J. T. Priestley, M. W. Comfort and R. P. Gage. Ann. Surg. 47:760-770 (May) 1958 [Philadelphia].

This study is based on 350 patients on whom total gastrectomy was performed during the years from 1917 through 1954. Most of these patients had gastric neoplasms, but a few had benign lesions. In this series of patients total gastrectomy was not employed as a routine procedure for a malignant lesion; it was performed for a malignant gastric lesion only when all involved tissue could not be removed by subtotal gastrectomy. During the last 15 years total gastrectomy has been used in approximately 18 to 20% of all patients who had gastric resection performed for cancer. Subtotal gastrectomy has been employed in the remainder. A majority of the 350 patients also had the spleen and omentum removed. The tail of the pancreas was removed only when neoplastic involvement was apparent in this region. Many patients had additional structures removed, such as portions of the diaphragm and colon and the left lobe of the liver when the malignant process extended to these regions. The ratio of males to females was approximately 2.5:1, and the average age of all patients was slightly more than 56 years, being identical for males and females.

Adenocarcinoma was the diagnosis in 85%, sarcoma in 5%, and benign ulcer in about 10%. Although the operative mortality rate associated with total gastrectomy has been reduced over the years, it has remained at 14 to 15% during the past decade, a percentage which is distinctly higher than that for partial gastrectomy. Leakage of the esophagointestinal anastomosis was the most frequent known cause of death. End-to-side esophagojejunal anastomosis between the jejunal limbs was used most frequently in restoration of gastrointestinal continuity. Seventeen per cent of the patients who had total gastrectomy performed for carcinoma survived 3 years postoperatively, 12% survived 5 years, 8.8% survived 10 years or longer. Slightly more than two-thirds of the patients who survived total gastrectomy for an appreciable period considered their health to be good.

Arteriovenous Fistula Involving the Abdominal Aorta: Report of Four Cases with Successful Repair. M. E. DeBakey, D. A. Cooley, G. C. Morris Jr. and H. Collins. Ann. Surg. 47:646-658 (May) 1958 [Philadelphia].

The fact that among 460 patients with aneurysms of the abdominal aorta treated by resection there were only 4 with aorta-vena caval fistula illustrates the relative infrequency of this fistula. In 3 of these patients the lesion was due to trauma and in 1 to a ruptured aneurysm. This latter patient was the only 1 in whom rupture occurred into the vena cava among the 44 patients with ruptured aneurysms in this series. The gravity of the arteriovenous fistula, involving the abdominal aorta and the inferior vena cava, lies in the hemodynamic disturbances produced by the fistula; the most important disturbances are those affecting the heart and resulting in cardiac enlargement and ultimately in high cardiac output failure. Accordingly, the primary objective of treatment is closure of the fistula, thereby arresting the hemodynamic disturbances and relieving the heart of its extra burden. A secondary objective is restoration of normal vascular continuity. Only in recent years has it been possible to attain both of these surgical objectives.

The authors present their experiences with the 4 patients, each of whom required a somewhat different method of repair to achieve both objectives. Analysis of these 4 cases, along with those previously reported in which surgical treatment was instituted, reveals that a majority of the cases were of traumatic origin and most of them occurred as a result of injury produced during previous operation for herniated intervertebral disk. Observations support the following conclusions: 1. Because closure of the fistula is the only means of correcting or preventing serious cardiac disturbances, immediate operative treatment should be instituted in all such cases. 2. A method of repair designed to restore normal vascular continuity, in addition to closure of the fistula, is highly desirable and should be possible in most, if not all, cases.

The Left Hepatic Duct and Its Usefulness in Repair of Damage to the Common Bile Duct. O. Hultén. Acta chir. scandinav. 114:355-360 (No. 5) 1958 (In English) [Stockholm].

The author used the left hepatic duct for plastic operations performed on 6 patients who were admitted to the surgical department of the University Hospital in Uppsala, Sweden, for repair of damage to the common bile duct; they had sustained their bile duct injuries in other hospitals where different kinds of plastic repairs had been tried. The patients had been ill with serious liver damage, and 1 patient had cholangitis with high fever and a severe infection. While the right hepatic duct appears on the cholangiogram as a direct continuation of the common bile duct and goes from the porta of the liver into the liver, the central part of the left hepatic duct lies free outside the liver or is covered only by thin parenchyma, so that one can dissect it and use it for a broad anastomosis with the jejunum in difficult cases of injury to the common bile duct in which nothing remains of the common hepatic duct. This technique was used by the author in these patients.

The course of healing was satisfactory, although occasionally bile flowed from the wound for a short time. The initial results thus have been good, but because of the comparatively short time which has passed since the operation, it is still too early for an evaluation of long-term results. The serious liver injuries found at operation heal slowly, even if bile flow to the intestine proceeds without hindrance. Autopsy performed on 1 patient, who died in hepatic coma, revealed multiple abscesses in the liver despite a well-functioning anastomosis. After-treatment of long duration is necessary, and the prognosis must be made with caution even if the operation itself is successful. Early operation is essential. The chronic and perpetually exacerbating cholangitis will otherwise lead to irreparable liver damage. If the right and left hepatic ducts run parallel for a long stretch, they can be damaged in such a way that one has 2 openings to provide for, which is an extremely difficult situation, but luckily this anatomic variation is rarely seen.

Albamycin in the Treatment of Surgical Infections. D. B. Nunn and E. F. Parker. Am. Surgeon 24:361-363 (May) 1958 [Baltimore].

Novobiocin (Albamycin), a relatively new antibiotic produced by Streptomyces niveus, was used in the treatment of 36 patients with infections observed on the general surgical service of the Medical Center Hospitals in Charleston, S. C. Four additional patients were given novobiocin prophylactically during the postoperative period. Of the 40 patients, 31 were given the drug orally, 1 received it intra-muscularly, and 8 were treated both orally and intravenously. In most patients, the oral dose was 250 mg. every 6 hours and the parenteral dose was 500 mg. every 12 hours. Cultures were obtained from 28 of the 36 patients with infections, and in vitro sensitivity tests were performed in all but 2 patients. Marked improvement occurred in 26 patients with gram-positive coccic infections; it was thought to be definitely related to the use of novobiocin. Improvement in 4 additional patients was believed to be due primarily to local treatment by incision and drainage, warm sodium chloride soaks, and mechanical débridement, rather than to the effects of the antibiotic. Six patients failed to improve after treatment with novobiocin. No evidence of infection occurred in the 4 patients in whom novobiocin was used prophylactically in the postoperative period. A skin rash, pruritus, and mild diarrhea were the side-effects which were observed in 6 patients. All side-effects disappeared within 2 or 3 days after discontinuation of the treatment. In vitro sensitivity tests performed on organisms isolated from the patients showed that novobiocin is effective in vitro against gram-positive cocci but has no significant influence on Proteus organisms. It would seem preferable to reserve the use of novobiocin for gram-positive coccic infections, in particular those due to staphylococcic organisms resistant to other antibiotics.

GYNECOLOGY & OBSTETRICS

Carcinoma in Situ of the Endometrium. J. I. Brewer. South. M. J. 51:554-560 (May) 1958 [Birmingham, Ala.].

Histologically, there is great similarity between those lesions in the endometrium and the adenomatous polyps of the colon and rectum which are variously designated as atypical epithelial hyperplasia and carcinoma in situ. Similarly, pathologists and clinicians vary in their opinions as to which lesion is atypical epithelial hyperplasia, which is carcinoma in situ, and which is actually carcinoma. Also, they differ in their opinions of the preferred method of treatment. At some stage in the development of adenocarcinoma there must be a stage which correctly can be termed carcinoma in situ. The author believes that the histological criteria for the diagnosis of carcinoma in situ elaborated by Hertig, Sommers, and Bengloff (an abstract of their paper appeared in The Journal 143:137 [May 6] 1950) are appropriate and correct. Hysterectomy is the procedure of choice but should be performed only under certain circumstances and with definite indications. In women aged less than 40 years, for whom it is urgent to preserve the uterus, curettage would suffice, provided that a second curettage would be performed electively 3 months later to determine whether the lesion has persisted or recurred. Follow-up examinations must be conducted for a long period of time, since it may be many years before invasive carcinoma develops.

Artificially Induced Female Pseudohermaphroditism. G. Nellhaus. New England J. Med. 258:935-938 (May 8) 1958 [Boston].

The case presented concerned an infant who was born at term of a 28-year-old gravida 4 who had a 6-year-old living normal daughter. A second daughter had died of pneumonia at 3 months of age, and the third pregnancy had terminated in a miscarriage in the latter part of the first trimester. To prevent another miscarriage, the mother was given tablets containing 0.04 mg. of ethinyl estradiol and 10 mg. of methyltestosterone. From the time of her first missed menstrual period for 100 days, when deepening of her voice caused the therapy to be discontinued, she took a tablet twice daily, or a total of 8 mg. of ethinyl estradiol and 2 Gm. of methyltestosterone. Labor was induced 1 day after the expected date of confinement. The parents were first told that they had a son with cryptorchism, hypoplastic penis, and hypospadias. Examination when the child was 7 days old disclosed that the labia majora were moderately enlarged, slightly corrugated and fused, but contained no palpable testicular tissue. There was a phallus, approximately 1 cm. in length, with a single opening at its base. A vaginogram, obtained by forcing of dye into the single perineal opening, showed a urogenital sinus with filling of the vaginal cavity and, separately and anteriorly, filling of the urinary bladder. Laparotomy, performed to determine the nature of the internal genitalia, disclosed an infantile uterus, oviducts, and cystic ovaries, wedge resections of which contained normal tissue. The parents were told that their child was a female and that she probably would mature in a normal manner. They were advised, however, that vaginoplasty would become indicated when she was old enough to understand and desire correction.

The author tabulates data on this and 5 other reported cases of artificially induced pseudohermaphroditism. The mothers of the other 5 infants also had received androgens during pregnancy and had experienced deepening of the voice, some hirsutism, and, in 1 case, marked irreversible enlargement of the clitoris. The androgenic effect of progesterone is also discussed, and it is suggested that a transient biological excess of progesterone may explain the cases of nonadrenal female pseudohermaphroditism in which a hormonal cause was not obvious. The recent occurrence of cases of artificially induced pseudohermaphroditism at a time when the use of hormones is widespread leads to the conclusion that androgenic hormones should be avoided during pregnancy, especially in the 3rd and 4th months, except in the most extreme circumstances. Moreover, whenever the question of sex determination arises in a newborn infant, a searching history of possible hormonal therapy during pregnancy is important as a guide to immediate diagnostic studies, therapy, and designation of gender.

Uncontrollable Obstetrical Hemorrhage. G. W. Jackson. J. M. A. Georgia 47:220-221 (May) 1958 [Atlanta].

Hemorrhage is one of the most common causes of maternal mortality in this country today. Afibrinogenemia, a depletion of the circulating blood fibrinogen, is a fairly frequent cause of maternal hemorrhage and occasionally death, occurring approximately once in every 1,000 deliveries. The suggested etiology for the depletion of circulating fibrinogen is threefold: 1. Thromboplastic material from the placenta, decidua, or amnionic fluid enters the circulation, causing intravascular clotting with depletion of fibrinogen. 2. Fibrinolytic enzymes enter the maternal sinusoids from necrotic decidua and destroy the circulating fibrinogen. 3. Depression of fibrinogen production in the liver is due to toxic fetal or maternal substances. The first of these is thought to be by far the most important. Predisposing factors associated with this condition during pregnancy or the postpartum period are premature separation of the placenta, presence of fetal death in utero, retained products of conception, and amnionic fluid embolus.

Afibrinogenemia should be considered in any obstetric hemorrhage. Numerous methods for determination of fibrinogen levels have been devised, with the normal values ranging from 300 to 700 mg. per 100 cc., and coagulation defects occurring with values in the range of 100 to 150 mg. per 100 cc. However, a simple, practical, and ample diagnostic procedure consists of placing 3 to 5 cc. of venous blood in a clean dry test tube and observing for clot formation and stability of the clot. In a normal individual the clot formed will be large and resist shaking. When fibrinogen is low, the clot is small and the blood watery, and the initial clot may readily lyse in minutes. The intravenous administration of fibrinogen is specific for this condition. It should be kept in every hospital that treats obstetric patients. Commercial companies supply 1-Gm. vials in the desiccated form which is stable under refrigeration for 5 years. The supply of the Red Cross is limited, as regards "on hand" stock, but it is suggested that hospitals participating in the Red Cross program keep at least 6 or 10 Gm. on hand.

Aortic Dissection in Pregnancy: A Case of Marfan's Syndrome. K. O. Husebye, H. J. Wolff and L. L. Freidman. Am. Heart J. 55:662-676 (May) 1958 [St. Louis].

The authors report on a 30-year-old woman with Marfan's syndrome, in whom aortic dissection occurred in the 22nd week of pregnancy. Repeated bouts of aortic dissection were observed from the 22nd throughout the 31st week of pregnancy, finally leading to the development of a triple-barreled aorta. Cesarean section was done electively 2 weeks before the expected date of confinement, and a normal male infant was delivered. After delivery no further attacks of dissection were recognized, but further cardiac enlargement occurred, and the patient's condition deteriorated. She died suddenly of congestive failure 13 months after the initial dissection of the aorta had taken place. Autopsy revealed chronic passive congestion of the lungs, liver, spleen, and gastrointestinal tract. Microscopic examination of the thoracic aorta revealed gross preservation of the elastic structures around the true aortic lumen. However, the elastic tissue seemed decreased in amount. The outer layer of the media with its elastic components could be traced into the outer layer of the wall of the channel caused by the aortic dissection, whereas the inner layer of this latter wall was greatly thickened and sclerosed with absence of elastic as well as muscle tissue. A high magnification from the wall of the thoracic aorta revealed not only a decrease in the amount of elastic tissue but also a focal disruption of the elastic laminas. The remnants of the elastic tissue formed clumps and irregular clusters, and the smooth muscle tissue seemed secondarily disorganized. Minor focal disruption of the elastic laminas, causing some retraction and clumping of the smooth muscle cells with minor disturbance of their circumferential arrangement, was observed in the abdominal aorta distal to the area of dissection.

At least 3 different factors, namely, hypoplasia of the aorta, Marfan's syndrome, and pregnancy, may have contributed to the aortic dissection in this patient. Dissecting aneurysm of the aorta in younger patients is characterized by an early degeneration of the elastic tissue components of the aortic medial layer, as is aortic dissection in pregnant women and in patients with Marfan's syndrome. After the degeneration of the elastic laminas, secondary changes are observed in the smooth muscle tissue, with ingrowth of numerous thin-walled vessels and development of cystic mucin-filled spaces, whereby the aortic wall becomes markedly weakened and susceptible to dissection. Both a disruption of the elastic fibers, as observed in the areas of aortic dissection in this patient, and a decrease in elastic tissue mass, as noted in the abdominal aorta distal to the dissection, may be characteristic histological features in Marfan's syndrome. Gestation enhanced the aortic dissection and shortened the patient's life.

Fifty additional cases of aortic dissection in pregnant women were collected from the literature; only 17 of these women went to term. Certain metabolic changes conducive to elastic tissue degeneration seem to take place in pregnancy. It is prudent to individualize termination of pregnancy in each case, depending on the stage of gestation at which the dissection occurs. Interruption of the early pregnancy is recommended as soon as the cardiac condition is stabilized. If possible, whenever the gestation is in the third trimester, the patient should be carried to viability of the fetus, and cesarean section should be the method of choice for termination of the pregnancy.

Carcinoma of the Fallopian Tube Simulating Acute Appendicitis: A Case Report. J. P. Mudd Jr. J. M. A. Alabama 27:312 (May) 1958 [Montgomery].

The patient was a 70-year-old woman who was hospitalized, complaining of severe lower abdominal pain and tenderness. The pain had started 14 hours prior to admission and was associated with nausea and vomiting; the woman had fainted once. Lower abdominal discomfort had been present for a week before admission. On auscultation, the abdomen was silent, and there was tenderness and rebound tenderness of the lower half. Rectal and pelvic examinations elicited extreme pelvic peritoneal tenderness. No masses were palpable. A milky fluid obtained by paracentesis was stained, and pus cells, but no bacteria, were seen. A celiotomy was performed for acute appendicitis. Upon opening the peritoneum, an odorless milky fluid was noted. The appendix, uterus, and left fallopian tube were normal. The right fallopian tube appeared greatly enlarged, hemorrhagic, gangrenous, and covered with a soft plastic exudate. This tube was removed and the abdomen closed. The pathologist made a diagnosis of grade 4 carcinoma of the fallopian tube. The papillary tumor developed within the lumen and apparently originated from the villi of the tube. The patient recovered after the salpingectomy but died 23 months later.

PEDIATRICS

Clinical and Biochemical Changes During Exchange Transfusion. J. W. Farquhar and H. Smith. Arch. Dis. Childhood 33:142-159 (April) 1958 [London].

Exchange transfusion is accepted as essential in severe hemolytic disease of the newborn, and it is carried out by operators of varying skill and experience. Some of the difficulties involved in blood transfusion are greatly increased by the volume of blood used in exchange transfusion. The infant may be perfused with stored blood of altered chemistry in quantities up to 3 times his own blood volume. Hazards, such as sepsis, air embolism, portal vein thrombosis, and perforation of the umbilical vein, have been described but are fortunately uncommon. Circulatory overloading is an ever-present danger in the profoundly anemic infant, and it may be precipitated by conducting the exchange transfusion too rapidly. Deterioration and even death may occur in infants whose preoperative condition gave rise to no concern. Such clinical deterioration was observed in as high as 40% of some of the reported series. In the belief that analysis of serum taken during exchange transfusion would reflect the ability of the newborn infant to maintain a normal serum electrolyte picture, the authors studied the electrolyte balance with reference to calcium and potassium ions. Of the 19 infants studied, 1 died during transfusion. Six others showed some clinically recognizable disturbance at some stage of the procedure. These included distal cyanosis, retching, shock, cardiac failure, and acute nonfatal collapse.

Hyperpotassemia was the only constant feature of the abnormal cases, and it was severe in the cases of cardiac failure, acute nonfatal collapse, and death. Three apparently normal infants, however, exhibited hyperpotassemia of similar magnitude. It is believed that none of the clinical incidents was due entirely to electrolytic imbalance, since similar biochemical changes were common to all the infants of the series. The depression of calcium ions can be neither prevented nor corrected by injecting calcium gluconate in the dose employed in this study. Other possible causes of clinical disturbance have been suggested, but evidence for them was not sought in this study. They include such factors as interference with the circulation during the period of postnatal readjustment, excessive speed of exchange, changing blood viscosity, manipulation of the catheter within the abdomen, the injection of cool blood, and, above all, inexperience on the part of the operator. There is more to the procedure than exchanging 10-ml. aliquots of blood. In a surgical team it is unlikely that an operation carrying a comparable mortality would always be left to the house surgeon or an inexperienced registrar. Yet junior staff may be left unsupervised to carry out an exchange transfusion in the belief, sometimes held by senior staff inexperienced in this procedure, that normal skill and common sense are all that is required. The apprenticeship to be served by the would-be operator of exchange transfusion is neither short nor easy, and even after many successes the experienced may be humbled by failure.

Treatment of Persistent Enuresis with the Electric Buzzer. I. G. Wickes. Arch. Dis. Childhood 33:160-164 (April) 1958 [London].

The treatment of enuresis was revolutionized when it was discovered by chance that an apparatus for signaling to parents that their child had a wet bed and needed changing also had the property of training the child to become dry. In the past 5 years more than 500 enuretic children have been referred to the author's outpatient clinic. Many of them responded to simple forms of therapy, and many others recovered spontaneously, but gradually a hard core of resistant cases accumulated. The latter patients were treated with an electric apparatus which consists of an alarm unit containing a buzzer, light, relay, and 6-volt battery, together with 2 flexible leads that can be clipped onto 2 fine metallic rectangular gauze mats, about 16 by 20 in. The mats are best secured on the bed by slipping each into a pocket, obtained by sewing a pillowcase to a drawsheet along its 3 closed sides to make a double open-ended pocket. The child, preferably devoid of pajama trousers, lies above the linen sandwich containing the mats. The alarm unit stands on a table or chair close to the bed and is switched on at bedtime. The alarm is actuated when the circuit is completed by urine that has soaked through the layers. Normally, a teaspoonful of urine will suffice to start the buzzer, and this, by awakening the child, will bring an end to micturition and will eventually, in favorable cases, prevent the act starting at all.

There were 100 children with intractable severe persistent enuresis, who were treated by this method of conditioning. The number included 81 boys and 19 girls, aged 5 to 17 years. A positive family history was obtained in 47 cases, and more distant relatives were enuretic in a further 28 cases, but the records were not all complete. Fifty patients responded rapidly and completely, 15 responded almost completely, 9 improved markedly but slowly, and 26 were failures. Relapses were mainly provoked by infections, sometimes by fatigue and anxiety. The marked improvement in the mental outlook of the children who responded was most gratifying. Several parents reported that their children were happier and more confident now that their enuresis had been eliminated. It is clear that a great deal of the associated anxiety was secondary to the enuresis and disappeared with it. There can be no doubt that psychological etiological factors have been greatly exaggerated in this disorder, although they certainly play a part in aggravating it. The author feels that in persistent cases of enuresis the conditioning method is justifiable and rewarding.

THERAPEUTICS

Treatment of Hypertension in Out-Patients: The Initial Assessment, and the Effect of Reserpine. R. Fife, J. P. J. Paton and W. G. Whyte. Scottish M. J. 3:165-172 (April) 1958 [Glasgow].

The purpose of this investigation was to find out whether a blood pressure of normal or near-normal levels could be maintained by oral drug therapy in a group of patients with fairly severe hypertension, who were fit to attend as outpatients and who, if possible, continued their usual occupations. After preliminary assessment, which included a period of at least 4 weeks with purely placebo medication, a standard regimen of treatment was followed with reserpine alone for a minimum of 6 weeks. Thereafter, if necessary, pentolinium was added, and if the response to it was unsatisfactory, it was replaced by mecamylamine. The reserpine was continued concurrently. Studies were made on 71 patients, and this paper reports the results after 6 weeks of reserpine therapy. A clinically acceptable fall in diastolic pressure occurred in about one-third of the patients, and the systolic pressure responded similarly. Normal levels of pressure were rarely produced by reserpine alone in the severe cases, although commonly in milder cases. The apparently superior results in milder cases were not due to a better percentage fall in pressure but to lower initial pressures. Reserpine is a useful antihypertensive agent, even in severe hypertension. After the preliminary placebo therapy, reserpine was given in a dosage of 0.5 mg. 3 times a day. The authors believe that the dose should, as a rule, be halved after a period of 4 to 6 weeks, even in the absence of side-effects, and that this reduced dosage may well turn out to be still too high for prolonged use in an appreciable proportion of patients. The side-effects from reserpine were the same as those recorded by other authors. Fluid retention, causing increase in weight and edema, was observed in many of the patients.

Early Observations on the Diuretic Effect of Oral Chlorothiazide. D. W. Davies and B. Evans. Brit. M. J. 1:967-969 (April 26) 1958 [London].

The effect of Chlorothiazide (6-chloro-7-sulfamyl-1,2,4-benzothiadiazine-1,1-dioxide) on the urinary output was observed in 8 women and 12 men, between the ages of 51 and 74 years, with clinical edema or pulmonary congestion from heart failure, who were given 1 Gm. of the drug by mouth twice daily for 4 consecutive days, followed by an interval of 3 or 4 days before a further course was started. Sixteen of the 20 patients received intramuscularly 1 or more injections of 2 cc. of mersalyl or mercaptomerin initially. The response obtained was measured as the diuretic index over a 2-day period. To compare the value of these diuretic agents, varying courses of intermittent therapy were used. Chlorothiazide produced a good therapeutic effect in all the patients. The results obtained suggest that it is as effective as the diuretics which are given parenterally, or more so. In the short and intermittent courses of treatment which were used, only a slight fall in the serum potassium level was determined in 5 patients; symptoms of hypopotassemia did not occur in these patients. The supplementary administration of potassium can possibly be avoided if administration of Chlorothiazide is interrupted by free periods, according to the procedure adopted by the authors. Toxic effects were not observed in any of the patients.

Perphenazine (Trilafon): New Ataraxicum. O. Lingjaerde and A. Schiøth. Tidsskr. norske lægefor, 78:278-281 (April 1) 1958 (In Norwegian) [Oslo].

A new tranquilizing drug, perphenazine (Trilafon), was given to 77 women patients, with placebo control. The patients were mostly chronic schizophrenics, with symptoms of restlessness, anxiety, negativism, autism, and apathy, who had responded poorly to previous treatment. The condition of 14 patients was definitely improved during the Trilafon treatment period. These results, together with later experiences with higher dosage, indicate that Trilafon is a valuable agent, effective in a number of patients who have not reacted favorably to other ataraxics. According to the degree of the symptoms, the treatment is started with a daily dose of 16 to 48 mg. of Trilafon (usually 24 mg.); depending on the therapeutic effect and the eventual side-effects, the dose is increased or diminished by 8-16 mg., usually at weekly intervals. The most prominent side-effects or drowsiness, fatigue, and sluggishness, but pyramidal tract symptoms have occurred in relatively many cases. The indications seem to be the same as for chlorpromazine and reserpine, but Trilafon seems to have a more stimulating effect on sluggish and apathetic patients. It is difficult to know which agent will be most useful in a given case, and for the time being one must feel one's way.

PATHOLOGY

A Serological Trial of Asian-Influenza Vaccine After the Autumn Epidemic. W. W. Holland, A. Isaacs, S. K. R. Clarke and R. B. Heath. Lancet 1:820-822 (April 19) 1958 [London].

A serologic trial of an Asian influenza vaccine was carried out in 83 volunteers, all of whom had been exposed to the autumn (of 1957) influenza epidemic. Thirty-three had had a clinical illness resembling influenza. Volunteers with no initial antihemagglutinin reacted poorly to a single dose of vaccine. A much better serologic response was obtained with a single dose in persons with initial titers of 1:5 or more. Two inoculations given to persons without initial antibody led to a good secondary response. This is contrary to previous experience, and it is suggested that 2 antigenic stimuli are needed to produce a good antibody response in persons who have not previously experienced this antigen, whereas 1 stimulus is probably sufficient for those that have.

Diabetic Retinopathy and Nephropathy in Pancreatic Diabetes. L. J. P. Duncan, A. MacFarlane and J. S. Robson. Lancet 1:822-826 (April 19) 1958 [London].

The etiological relationship of the vascular complications of diabetes mellitus to the disorder itself is the subject of much controversy. The view has been expressed that they may be determined by the same gene, since there are few reported cases of capillary lesions in diabetes due to pancreatitis or pancreatic fibrosis. The authors report here the development of diabetic retinopathy and of glomerulosclerosis of the type specific to diabetes mellitus in a patient whose diabetes is believed to have been due to chronic pancreatitis. In 1928, when the patient was 19 years old, the classical symptoms of diabetes mellitus developed. He was found to have glycosuria and was treated by dietary restriction and the administration of insulin. In 1936 he noticed that his stools were pale and floated in water and that he had lost weight. In 1947 he complained of episodes of nocturnal diarrhea, with passage of pale fluid feces. In 1952 he had neuropathy in his legs, with absence of ankle reflexes, diminution of knee reflexes, some wasting of the calf and adductor muscles, loss of appreciation of vibration and pain, and absence of sweating in the lower limbs. At this time diabetic retinopathy was first detected. Subsequently symptoms of urinary disturbances appeared. Courses of various antibiotics were given for urinary tract infections. In 1957 incontinence and recurrent infection became so severe that both ureters were transplanted to an isolated loop of ileum which acted as a reservoir, but in spite of this the patient died of urinary tract infection, toxemia, and uremia. At the time of death he had diabetic retinopathy.

During the 30 years of his diabetic life this patient frequently had hypoglycemic episodes, occurring up to 3 or 4 times a week, irrespective of the preparation of insulin used, and frequently requiring his admission to hospital. During 1 of these admissions, in 1955, pancreatic disturbances were recognized, and roentgenography disclosed extensive calcification of the pancreas. The analysis of the duodenal aspirate after the injection of secretin and pancreozymin confirmed the absence of exocrine pancreatic function. There was no family history of diabetes. The authors feel that the history of this patient constitutes strong evidence in favor of the view that the vascular complications of diabetes mellitus in the form of retinopathy and of glomerulosclerosis are the consequence of the metabolic disorder which results from insulin deficiency.

BOOK REVIEWS

Modern Trends in Endocrinology. Edited by H. Gardiner-Hill, M.D., F.R.C.P. Cloth. $13.50. Pp. 298; 13, with illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

The many advances in endocrinology of the past decade have made the appearance of this book particularly appropriate. It consists of contributions on the thyroid hormones by Pitt-Rivers, antithyroidal drugs by Dunlop, cause and treatment of exophthalmos and exophthalmic ophthalmoplegia by Gilliland, tests of thyroid function by McGregor and Wayne, treatment of toxic malignant thyroid disorders with radioactive iodine by Pochin, endocrine factors in diabetes mellitus by Randle, endocrine aspects of overnutrition and undernutrition by Kennedy and McCance, the pituitary antidiuretic hormone and the control of fluid balance by Black, new adrenal cortical steroids by Prunty, role of adrenal cortical and pituitary hormones in water and electrolyte control by Bayliss, adrenal cortical and other factors in hypopituitary coma by Caughey, the hormones in sympathetic nervous system of the adrenal medulla by Swan, adrenal function tests by Cope, cortisone and corticotropin in the treatment of rheumatic disorders by Savage, corticotropin and cortisone in the suppression of allergic and pararheumatic disorders by Hart, hormonal factors in breast development by Tindal and McNaught, endocrine factors in the cause and treatment of cancer of the breast and prostate by Stoll, endocrine treatment of gynecologic disorders by Bishop, endocrine factors in infertility in women by Bowes, carcinoid tumors in seratonin by Snow, and the stress concept by Rosch. As may be seen from this list, most of the book is devoted to the adrenal and thyroid glands. The editor has done an excellent job in organizing the present volume. The contributors have summarized all the pertinent advances of the past decade and presented their own critical evaluation of recent work and its implications for future investigations. Each chapter is followed by a list of recent references. The book is printed in an easily readable type and organized and arranged well. It can be recommended.

The Impact of the Antibiotics on Medicine and Society. Monograph II, Institute of Social and Historical Medicine, New York Academy of Medicine. Iago Gladston, M.D., editor. Committee: Frank J. McGowan, M.D., chairman, and others. Cloth. $5. Pp. 222, with illustrations. International Universities Press, Inc., 227 W. 13 St., New York 11, 1958.

This monograph deals with an event of epoch-making proportions in the history of medicine: the discovery and clinical application of the antibiotic drugs. In less than two decades, the antibiotics have revolutionized the practice of medicine and have deservedly attained the appellation, "miracle drugs." The 14 distinguished authors who contributed to this volume have discussed the historical development of the concept of antibiosis, the microbiology of the soil, the evolution of mass production methods for antibiotics, the use of antibiotics in plant husbandry and in the livestock industry, the influence of antibiotics on the clinical practice of medicine, and the impact of these drugs on public health and on society. The narrative style employed in most chapters makes this volume one which is rapidly and easily read. Since the language is, in general, nontechnical, this book should be of interest to laymen as well as medical historians, physicians, and workers in allied medical disciplines.

Endocrine Aspects of Breast Cancer: Proceedings of a Conference held at the University of Glasgow, 8th to 10th July 1957. Edited by Alastair R. Currie, B.Sc., M.B., F.R.C.P., Senior Lecturer in Pathology, University of Glasgow, Glasgow, Scotland. Foreword by C. F. W. Illingworth, C.B.E., M.D., Ch.M., Regius Professor of Surgery, University of Glasgow. Cloth. $8.50. Pp. 340, with illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland, 1958.

This symposium should command the interest of any clinician with more than a casual interest in cancer of the breast and should be of extraordinary interest to investigators and experimentalists of several disciplines with any concern in the relationship of neoplasia to endocrinology and steroid chemistry. The 88 contributors represent the United Kingdom, the United States, New Zealand, and various countries in Europe, including West Germany. The book's four parts deal with clinical aspects, pathology, hormonal studies, and experimental pathology. The part on hormonal studies is divided into three sections, the first on anterior pituitary hormones and mammotropins, the second on urinary estrogens, and the third on urinary 17-oxysteroids. Of particular value is the feature of a discussion and summary following each part and section, which are in the form of a critical commentary and which evaluate conflicting items of evidence. With perhaps one exception, these summaries provide a comprehensive, succinct orientation of such value as to justify the acquisition of the book for those who want up-to-date information with a minimum expenditure of time. At the end of the book is a review of the conference as a whole, an admirable statement of the outstanding reports and of some of the unsolved problems. Among the latter, from the clinical standpoint, the

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

selection of patients for ablative procedures is as yet unsolved, as is the choice of endocrine ablation (after oophorectomy). On the basis of up-to-date reports from most of the world's centers actively interested in such efforts, and subjected to thorough review at this conference, the comparison of the effectiveness of adrenalectomy versus hypophysectomy resulted in a verdict of "no decision." Equally in doubt are the basic reasons for objective response of some women with disseminated mammary carcinoma to alterations of hormonal environment, whether produced by administered steroid hormones or by ablative procedures. There is a distinctly greater frequency of objective regression following endocrine removal when there has been a previous response to administered hormones and also in those patients in whom metastasis did not appear until more than five years after the onset of the primary tumor.

The general summary of the clinical reports includes a statement that "a beneficial response in something approaching 50% of cases treated (by adrenalectomy or hypophysectomy)" is followed by a good remission lasting for a year or more in less than 25%. A review of the various reports indicates the necessity of a critical review of each report in respect to the exclusion of cases in calculating end results and in the interpretation of such words as remission, arrest, and regression. If a strict definition of objective regression is observed and those patients whose disease remains static are not included, the true rate of objective regression is something less than 40%. From the impressive volume of hormonal studies reported, there emerged only two biochemical indications of tentative practical value. The pretreatment urinary levels of gonadotropins were higher in women who were nonresponsive to treatment with diethyl, stilbestrol and irradiation of the pituitary, but these differences were essentially statistical, with much overlapping of readings. In the many studies of excretion patterns of urinary estrogens, there was a conspicuous absence of any notable difference in endogenous estrogen levels and in the metabolism of administered estrogens. There was no indication of any promising, practical pretreatment criteria of responders. The only contrast between controls without breast cancer and patients with breast cancer was in a higher proportion of estriol to total estrogens recovered after injection of estradiol. The latter finding seems to be nonspecific, having been found also in patients with myocardial infarction and in those with prostatic cancer. The methods used measured only the excretion of the classic estrogens (estrone, estriol, and estradiol-17β) and account for not more than 20 to 30% of the estrogen metabolites known to be present in urine. Adding further confusion to the general findings is the detection of significant amounts of estrogen metabolites in the urine of women after both adrenalectomy and hypophysectomy, with no correlation between the response of the disease and the presence or absence of such metabolites. On pages 150 to 153 appears in tabular form a review of the literature on hormonal assays in relation to human breast cancer that should be of great value to investigators with any interest in this problem. If there are any differences between responsive and nonresponsive patients in respect to estrogen metabolism, their demonstration will require detailed chromatographic analysis to obtain true metabolic patterns. Apart from such minutiæ as one's surprise over the use of "operate" as a transitive verb by a distinguished English surgeon, this book inspires great enthusiasm for the wealth of information it contains. It should serve as a chart for future efforts of clinicians and biochemists.

General Biochemistry. By Joseph S. Fruton, Eugene Higgins Professor of Biochemistry, Yale University, New Haven, Conn., and Sofia Simmonds, Associate Professor of Biochemistry and Microbiology, Yale University. Second edition. Cloth. $18. Pp. 1077, with illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16, Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1958.

This textbook differs somewhat in both organization and emphasis from most of the books on this subject which are now available. This is probably because it is intended to be used in the teaching of biochemistry to the biochemist and not in a course for the medical student or for students majoring in one of the allied sciences. This is not to say that the medical student or the chemist could not profitably use the book, but the clinical and organic chemical aspects are not stressed. Rather, the fundamental chemical activity of living matter—both plant and animal—is thoroughly discussed to provide adequate foundation for the proper understanding of many procedures in biology, pathology, and physiology. After the initial chapter on the scope and history of biochemistry, the authors have chosen to emphasize some fundamental aspects of protein, including general properties, electrolytic properties, structural units, and structure. Also included are chapters on metalloporphyrin proteins and nucleoproteins. Following these there are several chapters on the properties and kinetics of enzymes and on the various classes of enzymes, such as the dehydrogenases and oxidases. A series of chapters deals with various general and metabolic aspects of carbohydrates, fats, steroids, pigments, inorganic nitrogen, proteins, and amino acids. In addition to these there are single chapters on the metabolism of nucleic acids, the role of inorganic ions in metabolism, the hormonal control of metabolism, and a final chapter on vitamins and growth factors. Throughout the book there are appropriate references to a large number of books and monographs, and the book includes an extensive subject index.

Handbook of Treatment of Acute Poisoning. By E. H. Bensley, M.B.E., B.A., M.D., Director, Department of Metabolism and Toxicology, Montreal General Hospital, Montreal, and G. E. Joron, B.A., M.D., C.M., Assistant Physician, Department of Metabolism and Toxicology and Department of Medicine, Montreal General Hospital. Second edition. Cloth. $4. Pp. 212. E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland; Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2, 1958.

This book serves as a clear, simplified, practical reference for the general practitioner in the treatment of acute poisoning. It will perhaps enjoy an even wider use by others who are responsible for emergency treatment in cases of acute poisoning. such as nurses, first aid personnel, or even laymen. The book provides an excellent adjunct to basic instruction on the handling of poisoning in general and specifically in cases of those toxic compounds listed as most commonly involved. The grouping of poisons by types allows for a greater scope and coverage. While the book outlines the general course of treatment, it should be emphasized that individual cases should be considered carefully for variants from textbook descriptions and will, in many cases, necessitate the use of more specific treatment methods. No mention, for example, is made of the use of the artificial kidney in the treatment for acute barbiturate poisoning. A reasonably comprehensive check has been made on the efficacy of the drugs used from a pharmacological viewpoint, and the book has been found accurate. The general organization of the text is convenient. An appendix lists the requisites for a first-aid kit. An extensive bibliography adds to the value of the book.

Research and Education in Rheumatic Diseases: Transactions of the Second National Conference at National Institutes of Health, Bethesda, Maryland, December 1, 1956. Edited by Joseph J. Bunim, M.D., Clinical Director, National Institute of Arthritis and Metabolic Diseases. Sponsored by American Rheumatism Association, Arthritis and Rheumatism Foundation, and National Institute of Arthritis and Metabolic Diseases. Conference Committee: Currier McEwen, M.D., Chairman, and others. Published by Arthritis and Rheumatism Foundation in cooperation with National Institute of Arthritis and Metabolic Diseases, Public Health Service, U. S. Department of Health, Education, and Welfare. Cloth. Pp. 156, with illustrations. Arthritis and Rheumatism Foundation, New York, 1958.

This book is divided into three sections, the first of which deals with research on collagens and the ground substance in their physical, chemical, and metabolic aspects. The recent advances in immunochemistry, pathology, epidemiology, and clinical investigations in rheumatic diseases are discussed. The other two sections deal with the support that is available for research and training in rheumatic diseases and the graduate training program sponsored by the U. S. Public Health Service. Most of the scientific papers are accompanied by an adequate bibliography. The reproductions of the plates and graphs are good. The volume is well edited, with an excellent preface. This book should prove most valuable to the investigator and clinician interested in rheumatic diseases.

Pharmacology in Medicine: A Collaborative Textbook. Edited by Victor A. Drill, Ph.D., M.D., Lecturer in Pharmacology, Northwestern University Medical School, Chicago. Second edition. Cloth. $19.50. Pp. 1243; 30, with illustrations. Blakiston Division, McGraw Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England; 253 Spadina Rd., Toronto 4, Canada, 1958.

The second edition of this comprehensive textbook is a collaborative effort by 85 authorities in the field of pharmacology, 78 of whom also contributed to the first edition. The advantages of such a joint undertaking lie in the fact not only that each subject is presented by an authority but that the division of labor has permitted the appearance of a second edition within a period of four years. Despite the multitude of authors, the editor has succeeded in maintaining a uniformity of style and arrangement that facilitates the use of the book. A noteworthy addition is the excellent chapter by P. B. Dews on drugs affecting behavior. Improvements in format include the consecutive numbering of the pages throughout the book, rather than by chapters, and the inclusion of the author's name under each chapter heading. The book includes discussions of many of the newest drugs, and each chapter contains an adequate up-to-date bibliography.

Human Infertility. By C. Lee Buxton, M.D., Med. ScD., Professor and Chairman, Department of Obstetrics and Gynecology, Yale University School of Medicine, New Haven, Conn., and Anna L. Southam, M.D., Assistant Professor of Obstetrics and Gynecology, College of Physicians and Surgeons, Columbia University, New York. With chapter on endometrial diagnosis by Earl T. Engle, Ph.D., Professor of Anatomy, College of Physicians and Surgeons, Columbia University. Cloth. $7.50. Pp. 229, with 43 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

This book compresses, in a relatively small space, the problem of the infertile couple. Great emphasis is placed on the study of the male and female partners as a unit physically, endocrinologically, and psychologically. Diagnosis and the procedures used in subsequent treatment are thoroughly covered. The last two chapters are especially valuable, since they present the psychological and social significance of infertility frequently overlooked by the medical consultant. The book demonstrates the ways in which the experts explore the problem of infertility and arrive at conclusions which direct the therapy. It can be unreservedly recommended for the instruction of students and practitioners and as a reference book for specialists in the field of infertility.

situation will come under control, and the symptoms will abate. For the local treatment of the pruritus ani, the usual measures employed for this condition are indicated, including anesthetic ointments and dusting powders. Careful cleansing of the anal region with cool water is helpful. In general, the control of this condition depends on the discontinuance of antibiotic therapy and symptomatic measures for the control of intestinal irritability.

ROUTINE TESTS ON HOSPITAL ADMISSION

To the Editor:—*The staff of a small community hospital is concerned with the minimum requirements for laboratory tests in obstetric patients and in surgical patients being prepared for herniorrhaphy, hemorrhoidectomy, or such procedures as dilatation and curettage. What is the consensus of opinion on incorporation of routine chest x-ray and syphilis tests for these patients? Please give information on the medical aspects, as well as the medicolegal requirements.*

Allan Green, M.D., Fairfield, Calif.

Answer.—All obstetric patients, regardless of whether they are to be delivered in large hospitals, in small ones, or even at home, should have the following laboratory procedures: blood type and Rh factor determination, Kahn or Wassermann test, chest x-ray (preferably by means of a 14-by-17-in. plate rather than with use of a microfilm), red blood cell count, and hemoglobin level determination at the first visit and near term and repeated urine examinations. All patients admitted for minor operations should have the following examinations performed: complete blood cell count, urine examination, chest x-ray, and Wassermann or Kahn test. If the patient is anemic, the blood type and Rh factor should also be determined.

Answer.—The matter of minimal requirements for laboratory tests on obstetric patients or those to have herniorrhaphy, hemorrhoidectomy, or dilatation and curettage is a matter of the best judgment of the physician. As far as a hospital is concerned, the Joint Commission on Accreditation of Hospitals requires that all patients admitted to a hospital as inpatients should have a urinalysis and at least a hemoglobin level or hematocrit determination. It is understood by them that, even though it is a mandatory requirement, use of judgment still exists; an emergency delivery or an emergency operation voids this regulation if it is to the detriment of patient care. The law requires that a hospital exercise ordinary due care and judgment in the handling of its patients, and it would appear that this minimal requirement is justified. Anything else should be a matter of judgment by the physician. Routine chest x-rays and serologic tests for syphilis should also be matters of judgment by the hospital medical staff. If the type of hospital and community indicates it, they should be performed; if not, they should only be done at the discretion and judgment of the physician on the case.

Answer.—Routine tests, as a rule, should be discouraged; however, certain tests almost always should be included in the evaluation of an obstetric or surgical patient. Every patient who is to undergo general anesthesia should be given a complete physical examination, and a thoracic roentgenogram, determination of hemoglobin level, and urinalysis also should be done. For the obstetric patient, urinalysis should be performed once a month during the pregnancy. The hemoglobin level determination also should be made at frequent intervals, especially if the findings on any determination are abnormal. For both categories of patients, a test for syphilis usually is included. The feasibility of ordering this routinely may be questioned because of the infrequency of positive findings, but the hazards—medical and medicolegal —of missing a case are considerable. The attending physician may, at his election, omit certain roentgenograms or tests if he is well acquainted with the patient's medical history or if a complete examination has been made recently.

STEIN-LEVENTHAL SYNDROME

To the Editor:—*A 15-year-old girl has moderate facial hypertrichosis, menstrual irregularity, and obesity. Her father is mildly diabetic, and diabetes existed in the maternal and paternal grandparents. Hairiness is excessive in the pubic region and moderate on the face and extremities. Menarche began at the age of 12, but she had only three periods in 1957. She is inactive physically and a poor student. She has been taking 1 to 2 grains (0.05 to 0.13 Gm.) of thyroid daily off and on for two years. Her clitoris is normal, and results of rectal examination were negative. There are no striae. Her basal metabolic rate after the thyroid medication was discontinued for six weeks was −22%. Her blood sugar level was 90 mg. per 100 cc. and her cholesterol level 170 mg. per 100 cc. The 17-ketosteroids value was 8 mg. in 24 hours. The patient is particularly concerned with the facial hairiness. Would there be any value in attempting steroid therapy with a view to suppression of adrenal corticosteroid output? What is the prognosis in the Stein-Leventhal syndrome?*

Milton Vainder, M.D., Chicago.

Answer.—Steroid therapy should not be attempted unless there is evidence of adrenocortical hyperfunction by excessive excretion of 17-ketosteroids. The excretion of 8 mg. in 24 hours is not significantly excessive (normal adult female range, 5-14 mg. in 24 hours). Also, further diagnostic studies are indicated in this case. Hirsutism, irregular and diminishing menses, obesity, and slight elevation of the fasting blood sugar level are compatible with early Cushing's syndrome (adrenocortical hyperfunction). A glucose tolerance curve might be informative (diabetic type of disease without glycosuria). The circulating eosinophils are generally low. Probably most significant would be the determination of the level of plasma 17-hydrocorticosteroids, which is usually increased. There is also the possibility that this girl is hypothyroid and that the hypertrichosis is constitutional. As the basal metabolic rate determination may not be reliable, a chemical protein-bound iodine or butanol extractable iodine test should be done before considering more complicated diagnostic studies. The Stein-Leventhal syndrome (polycystic ovaries) is a good possibility in diagnosis (Stein, *Am. J. Obst. & Gynec.* 50:385, 1945). Hirsutism, amenorrhea, and obesity are usually present in this disease. 17-ketosteroid excretion is normal or only slightly increased, follicle-stimulating hormone excretion is normal, and estrogen activity is low. Pneumoroentgenography may be performed before considering either peritoneoscopy, culdoscopy, or exploratory laparotomy (Stein, *Am. J. Obst. & Gynec.* 50:385, 1945; Kunstadter and Tulsky, *Am. J. Obst. & Gynec.* 68:819, 1954). The technique is simple, and valuable information may be obtained as to the size, shape, position, and radiolucency of the ovaries, as well as the uterus. If the diagnosis of polycystic ovaries appears likely, laparotomy may be performed; if it is confirmed, wedge-shaped resection, as advocated by Stein and coworkers (*Am. J. Obst. & Gynec.* 58:267, 1949), may be done.

DIFFERENT BLOOD PRESSURE IN THE TWO ARMS

To the Editor:—*What is the significance, in a man 81 years of age, of a blood pressure of 180/70 mm. Hg in the right arm and 150/70 mm. Hg in the left arm? There is no evidence of active lung, pleural, or mediastinal disease. The cardiac and aortic shadows are within normal limits. The patient smokes 18 to 20 cigars daily, eats two meals a day, and otherwise appears to be in good health.*

W. Forest Dutton, M.D., Noel, Mo.

Answer.—A difference of 20 mm. Hg in systolic blood pressure in the two arms is within normal limits. A difference of 30 mm. Hg with a normal diastolic pressure in a man of this age is indicative of a narrowing of the innominate or right subclavian artery. Aortic arch syndrome and pulseless disease are possible diagnoses, but narrowing due to arteriosclerosis is the more likely cause of the difference in a man of this age. Additional studies are not recommended, because there are no symptoms and the chest x-ray finding is negative. This consultant is reluctant to suggest changes in the habits of elderly individuals who are otherwise healthy.

DETERMINING PRIMARY MALIGNANCY SITE FROM METASTATIC LESION

To the Editor:—*In dealing with metastatic lesions from various parts of the body, including lymph nodes, soft tissue, or bone, how often should the pathologist be able to determine accurately the primary site of the malignancy? The cases concerned with here usually present no definite primary site clinically or else an adequate history is not available. Histologically, some of these metastatic lesions are anaplastic and others show an acinar or papillary picture. Are there published statistics on this question, or would it be possible to give an estimate?*

M.D., Pennsylvania.

Answer.—Statistics offer no specific help in establishing the site of a primary carcinoma when a metastasis is submitted to examination. Several factors other than the specific histological structure of the metastatic tumor can contribute evidence in determining the probable site of the primary carcinoma. Among these is the distribution pattern of the metastases. Small carcinomas of the nasopharynx may cause no focal symptoms. The distribution of metastases into lymph nodes of the neck and the specific structure of the metastatic carcinoma in these provide full evidence for placing the primary site in the nasopharynx. This can be true of metastases from a symptomless carcinoma of the thyroid, those from an anaplastic small-cell bronchogenic tumor, and remote metastases from a hypernephroid carcinoma of the kidney, a cancerous pigmented nevus of the skin, a papillary carcinoma of the ovary, a mucinous or glandular carcinoma of the gastrointestinal tract, and so on with many other cancerous tumors. However, numerous carcinoma metastases in biopsies have a structure which suggests only several possible sites of origin. These sites should be listed in their order of probability. The above general comments apply to biopsy tissues removed for diagnosis. The problem of locating a small primary carcinoma occurs also in an autopsy examination. In both fields a large experience in the morphology of cancerous tissues is helpful, and in the autopsy meticulous attention to minutiae is basic. The percentage in correctly locating the primary focus on the basis of histological structure of a metastasis should be considered on the basis of (1) a specific tumor site and (2) all carcinomas. Among the specific carcinomas are some where, on the basis of histology in the metastasis, the accuracy can approach 100%; of others the range is all the way to 0. The percentage for all tumors requires statistics from many laboratories in order to cover the total range of tissue samples. The average of these would be an answer, but, after all, not specifically helpful.

EPILEPSY AND LOW BLOOD SUGAR LEVEL

To the Editor:—*Two years ago, an 18-year-old boy was thrown clear from an open car. He was dazed for a few minutes but was able to walk away from the scene of the accident. Several months later he had a serious case of infectious hepatitis, from which he apparently recovered. However, this was followed by the development of typical epileptic seizures—though an electroencephalogram done at that time was reported to be normal. Treatment with 6 grains (0.39 Gm.) of diphenylhydantoin sodium and 3 grains (0.19 Gm.) of phenobarbital per day was ineffective. A neurologist has declared that a recent electroencephalogram was typical for epilepsy. All the patient's "spells" occur in the fasting state and always in the morning. He can, however, skip a meal easily without any ill effects and without inviting any trouble or seizures. The boy was very much depressed, in part, at least, because of the medication. His basal metabolic rate was —26%, and his school record was poor. Substitution of thyroid extract for the previous medicaments changed the picture; avoidance of any long period of fasting and breakfast in bed has so far abolished any seizures. His blood sugar levels have varied between 60 and 80 mg. per 100 cc., no matter when they have been taken—at the time of his awakening in the morning, before his breakfast in bed, and shortly after breakfast (consisting of toast, coffee, eggs, and bacon). They even stayed within this range after a tolerance test with 100 Gm. of dextrose was done. What is the explanation of this peculiar pattern of blood sugar level? At no time did the level dip low enough to suggest the diagnosis of hyperinsulinism. What else can be done to confirm or deny the diagnosis of epilepsy?*

M.D., New York.

Answer.—The diagnosis of epilepsy rests primarily on the description of the seizure, which is not given. The abnormal electroencephalogram is supportive, but here again a description of the abnormality would be helpful. Around the time of waking is a favorite time for seizures, whatever the cause, to occur. To be significant, the blood sample should be taken at the onset of a seizure. A more profound hypoglycemia induced by the injection of insulin might bring on a convulsion. Any blood sugar curve should cover a period of five hours. It seems unlikely that a blood sugar level at the lower edge of normal and the seizures are related. The question, then, is the cause of a consistently rather low blood sugar level. A functional hypoglycemia may be related to dysfunction of liver or thyroid. This patient has a history of jaundice and low basal metabolic rate. Diabetes may accompany hyperthyroidism, and, conceivably, the reverse condition might exist here. The present freedom from attacks is due more likely to the use of thyroid than to having breakfast in bed. Repetition of the metabolism test and of the electroencephalogram would be in order. The book "Diagnosis and Treatment of Convulsive Disorders in Children" by Livingston (Springfield, Ill., Charles C Thomas, Publisher, 1954) gives background information.

TREATMENT OF MANSON'S SCHISTOSOMIASIS

To the Editor:—*Please give advice on treatment for relapse of Manson's schistosomiasis in a 2-year-old girl weighing 29 lb. (13.2 kg.). She has previously been treated with stibophen, given intramuscularly for a total dosage of 16.65 cc.*

David R. Edwards, M.D., Sedalia, Mo.

Answer.—The inquiry makes no reference to the source of infection, number of ova per gram of feces, enlargement of spleen and liver, presence of ascites, or severity of symptoms. There is no highly effective, well-tolerated drug for the treatment of schistosomiasis. Nevertheless, two kinds of drugs are available to the practitioner: 1. Antimonials, such as antimony sodium tartrate, stibophen, and antimony lithium thiomalate, kill adult worms as well as ova. 2. A thiaxanthone, miracil D, kills primarily adult schistosomes. It is most effective against Schistosoma haematobium, less effective against S. mansoni, and ineffective against S. japonicum. Antimony sodium tartrate is still regarded as the most effective antimonial. Its use is recommended provided that the patient does not have ascites and the liver is not markedly cirrhotic. It should be administered intravenously and very slowly. A long or short (one to three days) therapeutic regimen may be chosen. The likelihood of severe systemic reactions, including fatality, is much greater with the short course of therapy. For the long course the dose is 2 mg. per kilogram of body weight, given on alternate days. With a 1% sterile solution of antimony potassium tartrate (tartar emetic), the dosage regimen for this child should be 1 ml. on the first day, 1.5 ml. on the third, and 2 ml. on the fifth, thereafter, 2 ml. on alternate days until a total of 18 injections are given. The cure rate is about 90%. Commonest side-effects are cough, vomiting, thoracic, abdominal, muscular, and articular pains, reversible inversion of T waves on the electrocardiogram, and urticaria. Urticaria may be due to reaction from the drug or to destruction of parasites. Miracil D is available in the form of 0.2-Gm. tablets. The dosage is 6 to 20 mg. per kilogram of body weight per day for 8 to 20 days. The course of treatment may be repeated. For this child, the administration of one-half tablet after breakfast and supper is recommended. The cure rate with this drug is 20 to 50%. Simultaneous administration of 5 drops of belladonna tincture and dimenhydrinate may reduce the intensity of side-effects, which consist of anorexia, nausea, vomiting, vertigo, tremors, insomnia, headaches, pruritis, yellow discoloration of skin and, occasionally, cutaneous eruptions.

EAR DAMAGE AND THE TELEPHONE

To the Editor:—*A woman, aged 34, was recently conversing on the telephone with a neighbor during a storm. The patient was soon after found on the floor, and the telephone was "dead." Examination revealed a large polygonal shaped perforation of the tympanic membrane and reduced hearing. Thirty-six hours later the patient had a serosanguinous discharge from which hemolytic streptococcus was isolated. From the onset, the patient experienced a severe vertigo which has persisted to the time of writing (eight days). A nystagmus is present and fairly marked, but diminishing. On the seventh day after the alleged injury the patient developed a mild facial paralysis on the same side. Are there any cases on record of a patient receiving an injury transmitted through a telephone during an electrical storm?*

Ben K. Williamson, M.D., Moline, Ill.

Answer.—Telephones usually are well grounded. Accidents with or without personal injury are rare. In the absence of grounding for any cause, and occasionally in the presence of grounding, electric storms may do damage, chiefly to telephone instruments. When persons are injured, the cause usually resides in high-level and, commonly, high-frequency sound and is not a direct effect of lightning. Such high-sound energy as a concussion or an impact effect may rupture the tympanic membrane and induce partial deafness and vertigo. The discharge of firearms in proximity to the ear is also a frequent cause. The initial damage here described is consonant with noise injury. The sound required could be transmitted by the telephone, originating nearby or far away in relation to lightning phenomenon. On the other hand, the telephone was not necessarily involved in the causation. A high intensity clap of thunder in the immediate vicinity could have produced the damage. In that instance injury to both ears would have been an increased prospect. The assumption is that the ear against the telephone receiver was the one damaged. The subsequent developments of nystagmus and facial paralysis may not be attributed to direct sound-energy effects; such may relate to the secondary infection mentioned. If a direct stroke of lightning were involved, with damage to the household telephone instruments, that fact would be known to the telephone company and might appear in the repair record.

TOXICITY OF FLUORESCENT TUBES

To the Editor:—*The injurious effects of beryllium on contact or inhalation have been known for many years. What chemicals are used in the manufacture of the present-day fluorescent tube? What toxicity is present on topical or oral contact? What measures should be taken if a patient accidentally takes food contaminated with any of the toxic material?*

J. E. B. Ziegler, M.D., Eau Claire, Wis.

Answer.—At the present time major producers of fluorescent lighting tubes make no use of beryllium, and not since 1949 has this been the case. However, it is suspected that many smaller and petty manufacturers of such tubes still may be using beryllium on an irregular basis. This is more likely to be true of the sign type of tube, since in the complex bending of such tubes presently employed phosphors tend to drop off or to crack. The occurrence of some cases of beryllium poisoning from fluorescent tubes at the present time should not be regarded as impossible. While there are many guarded trade secrets in lamp phosphors, it is known that the current commoner ones are zinc silicate, calcium lead tungstate, calcium lead manganese silicate, and calcium lead silicate, with an occasional use of magnesium arsenate and equally rarely of an antimony salt. It is possible that some calcium phosphates may be utilized. The manufacturers discourage the use of arsenic phosphors because of possible damage to humans. The use of lead is carefully safeguarded among major manufacturers. It is unlikely that any damage from lead would arise in connection with a single broken tube, such as was the case when beryllium was in wide application. There are good reasons to believe that the chief locus of damage to workers from phosphors is in the small shops, which exist by the hundreds but wherein some phosphors are made under crude manufacturing conditions. In connection with some fluorescent tubes small quantities of metallic mercury may be introduced, but such mercury is for purposes apart from that of the true phosphors.

REMOVAL OF HEMANGIOMA

To the Editor:—*Please give information on present methods of removing a hemangioma. Is removal by dry ice, liquefied carbon dioxide, and x-ray considered a surgical or a medical procedure?*

John H. Patterson, M.D., Boise, Idaho.

Answer.—The method of choice for removing a hemangioma depends on the lesion. A selection of modality must be made according to the size, onset. This view is endorsed by Alexander and associates (*J. A. M. A.* 166:1943-1949 [April 19] 1958). It is relevant that these workers agreed with numerous other observations that the naturally occurring and the synthetic corticosteroids were not as effective as corticotropin.

ALUMINUM HYDROXIDE AND DIETARY PHOSPHORUS

To the Editor:—*What dosage of aluminum hydroxide gel is necessary to precipitate or remove an adequate amount of dietary phosphorus from a parturient's diet when this includes 1 qt. of milk daily?*

Benjamin E. Morgan, M.D.
Rocky Mount, N. C.

Answer.—Because of the many variables and interrelationships involved, it is impossible to give a categorical reply to this question. In the first place, the amount of aluminum hydroxide present in various brands of aluminum hydroxide gel varies, and, in the second, of the 900 mg. of phosphorus in a quart of milk, about 80% is in the inorganic form, which presumably would be that which would react with the aluminum hydroxide. The amount available for reaction would also depend on the other foods present in the stomach, along with the amount of hydrochloric acid present.

PAGET'S DISEASE (OSTEITIS DEFORMANS)

To the Editor:—*What would be the treatment for a 44-year-old patient with Paget's disease involving the sacrum and left femur? He has few, if any, symptoms. On May 11, 1956, his serum alkaline phosphatase level was 7.4 Bodansky units per 100 cc., and on April 15, 1958, it was 12.4 units per 100 cc.* *M.D., Georgia.*

Answer.—The treatment for Paget's disease (osteitis deformans) is symptomatic. There is no known effective therapy. If the patient complains of pain, small doses of phenylbutazone will be effective in relieving the discomfort. One 100-mg. tablet of this drug each morning and evening has proved to be more effective than any other medicament known to this consultant. Approximately 5% of patients with this disease develop sarcoma in the affected bone. A checkup x-ray every 12 months is a justifiable precautionary measure.

HEADACHE REACTION TO SULFONAMIDES

To the Editor:—*What is the physiological explanation for headaches that frequently accompany the internal use of sulfonamides?*

J. Richard Allison Jr., M.D., Columbia, S. C.

Answer.—Headache is not generally considered to be a common complication of sulfonamide administration. However, should it occur, it is likely that hypersensitivity is a possible explanation. Mental disturbances have been described, and vague "neuritides" are sometimes encountered. The exact mechanism is not known, and the occurrence is usually unpredictable. Mild, transient reactions have been more frequently observed in persons in poor health but were found infrequently in personnel of the U. S. Navy during World War II (Thomas, *J. A. M. A.* 126:490-493 [Oct. 21] 1944).

VITREOUS OPACITIES OF THE EYE

To the Editor:—*In the answer to the question on vitreous opacities of the eye, which appeared in* The Journal *for April 5, 1958, page 1802, the consultant suggested vitreous implantation as a cure for an eye with better than normal vision. This procedure is completely at variance with sound ophthalmological practice, and the question should be reopened.*

Gordon M. Bruce, M.D.
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New York 32.

To the Editor:—*A comment on the answer to the question on vitreous opacities of the eye* (J. A. M. A. 166:*1802 [April 5] 1958) is in order. First, as to the chronic conjunctivitis, this is probably not related to the amebic colitis. The latter should, of course, be treated for its own sake, but a more rational approach to the treatment of the conjunctivitis would be to make smears and cultures of scrapings of the conjunctiva. This should include examination for fungi. Sensitivity tests should then be made on any organisms recovered and the appropriate antibiotic prescribed. In many cases chronic conjunctivitis is part of a blepharoconjunctivitis, and in these patients treatment of the scalp, as well as of the lids, with a selenium sulfide preparation is of benefit. The vitreous opacities are a completely separate problem, and in a patient with normal (in this case better than normal) vision the surgical intervention suggested is absolutely contraindicated. Transplantation of vitreous is fraught with danger, and in every case a hole must be produced in the choroid and retina. The risk of hemorrhage and retinal detachment is obvious. In a patient with "30/20 vision" the opacities can only be considered an annoyance and not a true problem. There is no scientifically acceptable treatment for vitreous opacities. One can only examine the fundi carefully to rule out lesions of the retina. Such a careful examination, plus a strong assurance on the part of the physician that the eyes are normal, often completely alleviates the patient's anxiety and makes him less aware of his "floaters."*

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WASHINGTON NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

New Medicare Regulations Limit Civilian Phase of Program . .
House Committee Proposes Changes in VA Hospital Policies . .
FTC Accuses Drug Companies of Price-Fixing: Charges Denied . .

CHANGES IN MEDICARE OUTLINED TO STATE MEDICAL SOCIETIES

The Army, administrator of Medicare for the three services, has announced the outline of changes to be made in Medicare at the insistence of Congress that more dependents be cared for in military hospitals.

Proposed restrictions were discussed at a Pentagon meeting to which were invited representatives of state medical societies, Blue Cross, American Medical Association, American Hospital Association, and Mutual of Omaha insurance company.

While not all details had been worked out, the Army said the restrictions would be about as follows:

1. All dependents residing separately and apart from their sponsors will have complete free choice of civilian physicians and civilian hospitalization or medical care in military politics.
2. In remote areas, the commanding officer will be authorized to grant permission for dependents to use civilian facilities.
3. In certain metropolitan areas—including Washington, D. C., Denver, and San Francisco—a central clearing office will be established to determine what military facilities are available. At the clearing office dependents will obtain certificates authorizing civilian care if it is determined that the military facilities in that area cannot handle the particular case.
4. Certain present authorizations for care by civilian physicians and hospitals will be eliminated. These include well-baby care, outpatient care for fractures and dislocations, etc.
5. All dependents residing with the sponsor must use military facilities, with the following exceptions: If military facilities are unavailable or scheduled to be filled to optimum capacity (optimum capacity will be based on the present or existing capacity at the time the Medicare program began). The dependent will receive a certificate of entitlement or authorization to use civilian physicians and civilian hospitalization.
6. In maternity cases, if the patient is living with the sponsor and is in the first trimester she must either change to military facilities or obtain certification of nonavailability of military facilities. If in the second or third trimester, she may continue to receive civilian care.

Meanwhile, Congress at this writing has about completed action on the Defense Department's appropriations bill, where Medicare difficulties first appeared.

In the House, the Medicare appropriation was reduced from a requested $70,200,000 to $60,000,000, and stipulation was written into the bill that would prevent the Defense Department from exceeding this total for the civilian program. These restrictions were voted in the face of a Defense Department estimate that Medicare would cost close to 100 million dollars. Had the restrictions been sustained in the Senate, Medicare would have had to be scrapped and a new program, severely limited in scope, set up, according to Defense Department.

After lengthy hearings followed by closed-door debate on Medicare, the Senate Appropriations Committee sustained the House, Medicare was in jeopardy, with the last hope of saving it resting on the Senate vote.

Before the vote came, a personal letter was sent to every Senator by Dr. William J. Kennard, acting director of the Washington Office of American Medical Association. After summarizing the situation, the letter declared that if the restrictions were not lifted there will be many thousands of service families living in parts of the country where no military hospitals are located who will be denied the medical benefits Congress has pledged them. The numbers of such families will definitely increase in the next year because of the need for more combat troops overseas and the strong possibility that many dependents will be evacuated from certain overseas areas. If costs of the civilian program are to be cut 60% (as the bill requires), these people will have to be deprived of many medical benefits.

Dr. Kennard's letter also called attention of the Senators to a Defense Department report dated last May 5, which was presented to neither Senate nor House appropriations committees when they were considering the Medicare appropriation. This quotation from the report was cited:

"It is the consensus that the hospitalization cost in the military hospital system would be approximately the same as that in the civilian hospital system if it were possible to compute the total cost of both systems on the same basis." (Robert McCullough, representing the defense Comptroller, has stated that in his opinion the costs in military hospitals could be higher.) The same report also states: "The military could not possibly take care of the thousands of dependents who are going to civilian hospitals and being cared for each day under the Medicare program."

The fight on the Senate floor to eliminate the House restrictions was led by Senator Knowland (Calif.), Republican leader, who reviewed all facts in the problem and emphasized that Medicare had been a success and should not be dropped.

Just prior to a vote on the Knowland amendments, Senator Chavez (D., N. M.), chairman of the Defense appropriations committee that had approved the House restrictions, said he now was prepared to support their elimination, in view of Defense Department promises to channel more dependents to military facilities.

The amendments then were adopted by a voice vote, and although a large number of Senators were on the floor in anticipation of a final vote on the defense appropriations, only one or two "nays" were heard against the amendments.

Shortly after the Senate's action, House members of the conference committee agreed to support the Knowland changes, which restored the Medicare fund to $70,200,000 and made it possible for Defense Department to supplement this fund. The conference committee report then cleared both Senate and House with very little discussion and was sent on its way to the White House for certain approval.

VA HOSPITALIZATION BILL INTRODUCED

Introduced too late for action this year, a bill receiving the full backing of the House Veterans Affairs Committee would write into law for the first time a specific number of Veterans Administration beds. It also would spell out admission procedures aimed at non-service-connected patients unable to pay for care.

Actual target of the measure sponsored by Rep. Olin Teague (D., Tex.), committee chairman, is the Budget Bureau. The committee maintains that administrative decisions imposed on VA have resulted in curtailment of hospital facilities. More specifically, some 5,000 VA beds are not being used, according to the committee.

The bill would do the following:

1. Direct VA to operate 125,000 beds for an average daily patient load of 113,000. Present figures are 120,526 operating beds and 111,000 daily load.
2. Write into law, as first proposed in H. R. 58, the 10-P-10 form which veterans with non-service-connected illness now sign on entering VA hospitals; it gives their financial status. This section also requires reading to the applicant of the criminal code pertaining to false statements under oath.
3. Require VA to notify the Veterans Affairs Committee during a session of Congress, and at least 90 days in advance, of any plans to shut down a hospital or other VA facility.
4. A VA administrator could refuse to furnish hospitalization to non-service-connected veterans who are eligible under workmen's compensation, industrial accident laws, or health insurance plans, if other eligible veterans are waiting for care. The restriction would not apply in emergency cases.
5. Authorizes the administrator to furnish outpatient care for non-service-connected cases where necessary to determine if admission to a hospital is required and where essential to complete treatment incident to hospital care.

The committee is particularly interested in seeing that general medical and surgical hospital beds are used for selected mental patients.

However, in the last several years the transfer of such patients has dropped off. Comments the committee: "This apparently is pursuant to the administrative decision imposed on Veterans Administration that its program for the care of the long-term chronic or intermediate type patient will not be expanded."

On the inability-to-pay form, the committee comments: "It is apparent that, in each instance where a veteran seeking care for a non-service-connected disability misrepresents his ability to pay, an illegal expense is borne by the taxpayers and an eligible veteran is deprived of the use of the bed occupied by the ineligible person. It is believed that this bill will assist the Veterans Administration in dealing with the relatively few cases of abuse which confront it."

DRUG FIRMS CHARGED WITH PRICE-FIXING ON TETRACYCLINES

The Federal Trade Commission has charged six drug companies with price-fixing on a number of antibiotics, and the firms have promptly denied the charges. The FTC charges that "for many years" all six companies had "fixed and maintained arbitrary, artificial noncompetitive and rigged prices" for the three tetracycline drugs.

The companies named in the complaint are Charles Pfizer & Co. Inc.; American Cyanamid Co.; Bristol-Myers Co.; its subsidiary, Bristol Laboratories Inc.; Olin Mathieson Chemical Corp.; and the Upjohn Co. According to an accompanying 361-page report titled "Economic Report on Antibiotics Manufacture," American Cyanamid is identified as the largest producer, in 1956, of antibiotics; Pfizer is second, Mathieson fourth, Upjohn sixth, and Bristol-Myers ninth, out of 12 companies. Sales of all antibiotics that year were estimated at 330 million dollars.

The FTC claims that Pfizer had made "false, misleading, and incorrect statements to the United States Patent Office" in order to induce it to grant a patent on tetracycline even though FTC claims there was "no real novelty or invention in the claims of the patent." The complaint said that Pfizer then issued "invalid licenses" under the patent, starting with Cyanamid in 1955, then Bristol Laboratories, Olin Mathieson, and Upjohn in 1956.

The FTC gave the companies 30 days in which to respond to the complaint. A hearing on the whole subject has been set for Oct. 1 in New York City at which time the firms may show cause why an order should not be entered requiring them to cease and desist from violations of the law charged in the complaint.

THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 16 CHICAGO, ILLINOIS AUGUST 16, 1958

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PRODUCTION OF MEDICAL PERSONNEL THROUGH VOCATIONAL REHABILITATION

Jean S. Felton, M.D., Oklahoma City

The cost and results of rehabilitation programs are presented in order to correct the erroneous idea that patients who have been rehabilitated enter only the fields of crafts and custodial or protective work. In reality, the rehabilitative process also increases the number of professional workers. This paper reviews 20 years of experience in the Oklahoma State Division of Vocational Rehabilitation with reference to the paramedical occupations. The group of patients prepared for active professional life included, among others, 35 laboratory technologists, 26 nurses, and 17 physicians. The cost of their rehabilitation has been estimated and compared with the estimated earnings and anticipated income tax payments of the group. It is believed that the return to the government from this investment is about sixtyfold. To this must be added the special benefits accruing to society from the development of needed professional skills, the restoration of human dignity, and lessened need for public assistance to older people.

As a RESULT of the repetitive and vast demands for manpower during World War II two operating principles of vocational rehabilitation became prevalent in America. The first was the conservation and improvement of all human resources and the other the utilization of the physically impaired in productive work. The limited needs for personnel at home and abroad in 1917 were of insufficient dimension to emphasize the potential role of the handicapped. However, war's aftermath of injured and ill brought about the passage of the first enabling legislation in the area of vocational rehabilitation.[1]

The program remained a somewhat narrow-gauge undertaking until the newer concepts of holistic care emerged from armed services' medicine toward the end of World War II. With the impetus given by the dignity-restoring measures of the Army and Navy hospitals in amputation, paraplegia, and plastic surgery centers and with the lessons learned from the employment of the handicapped in our wartime plants, businesses, and utilities, American medicine and industry underwent a reorientation of the needs and proved capacities of the physically marginal person. Supported through additional congressional measures,[2] the Office of Vocational Rehabilitation in the Department of Health, Education, and Welfare has aided

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Professor of Preventive Medicine (Occupational Medicine), University of Oklahoma School of Medicine.

the states in restoring great numbers of citizens to effective states of production—demonstrating that with good and complete medical care, training, and placement, the person burdened with disease or injury residua could establish his place in the sun. (In the fiscal year 1955-1956, 65,640 persons were rehabilitated through the Office of Vocational Rehabilitation program, and 221,156 were rendered service.[3])

Unfortunately, many noninquiring groups have believed this effort to be unrelated to the creation of professional workers but concerned solely with the development of custodial, craft, or protective employees. Further, one often encounters voiced opinions that this is another step toward state control of professional activities. My objective in this article is to demonstrate the broader scope of vocational rehabilitation services and to point up the wisdom of investing small sums of federal and state money for a gain in the creation of physicians, nurses, and paramedical personnel and for the return of considerable tax moneys to national and state treasuries.

TABLE 1.—*Medical and Paramedical Personnel Rehabilitated by Year*

Yr.	Persons, No.
1937-1938	3
1938-1939	7
1939-1940	3
1940-1941	3
1941-1942	6
1942-1943	11
1943-1944	...
1944-1945	11
1945-1946	13
1946-1947	7
1947-1948	7
1948-1949	6
1949-1950	19
1950-1951	14
1951 1952	4
1952-1953	24
1953-1954	24
1954-1955	9
1955-1956	13
1956-1957	6
Total	190

A Case Load in Review

To determine the worth of a rehabilitation service program in the single area of medicine, the records of a 20-year period, 1937-1957, were reviewed in the Oklahoma State Division of Vocational Rehabilitation (DVR), and basic extrapolations were carried out which would permit a delineation of the persons given care, trained, and placed and would give an understanding of the financial accruals to tax-collecting agencies during the projected working lives of the rehabilitated clients. The DVR in this state functions similarly to all comparable agencies in that it is engaged "in rehabilitating physically handicapped individuals so that they may prepare for and engage in remunerative employment to the extent of their capabilities, thereby increasing not only their social and economic well-being, but also the productive capacity of the Nation. . . ."[4] To reach this goal, the DVR provides diagnostic and related services incidental to eligibility determination, training, guidance, and placement services. To correct or modify a physical condition which constitutes a substantial handicap to employment, corrective surgery or medical or psychiatric care is provided, along with hospitalization, prosthetic devices, maintenance during rehabilitation, prevocational, physical, and occupational therapy, and adjustment training. These comprise an "integrated program of medical, psychological, social, and vocational evaluation and services under competent professional supervision."[5] In some instances equipment and initial stocks and supplies for the establishment of a small business or vending stand are provided, but rarely was this type of service applicable to the group being considered.

This program results in manifold benefits—to the client who becomes gainfully employed, to the hospital which has an additional "paying" patient, to the physician rendering the surgical or medical care, to the employer who gains a worker, and to the federal and state governments which then will receive income taxes from the working rehabilitee.

Although the DVR cared for 18,706 clients during 1937-1957, only those persons relating to medicine or the paramedical occupations will be considered. This group comprised 1.01% of the total. In table 1 are shown the numbers of clients rehabilitated in the various medical occupational catagories. There were 89 men and 101 women in the group, from 18 to 64 years of age.

The postwar years saw a great acceleration in the numbers of clients rendered service, and, whereas those rehabiliated prior to World War II averaged 4 per year, the number increased after this to a mean of 11 per year, with a high point of 24 yearly during the period of 1952-1954, during and after the termination of the Korean conflict.

Table 2 depicts the occupational categories selected by the clients receiving service and shows the distribution by disability. Tuberculosis led the group with 42 clients (22.1%), poliomyelitis residua marked the second most frequent condition, with 25 (13.2%), and the third was bone and joint disorders, with 20 (10.5%). The largest single category of personnel rehabilitated was laboratory technicians (35), with professional nurses and practical nurses second at 26 each; dental technologists were third (18), and 17 physicians were fourth in the group. It is of interest that 26 (62%) of the former tuberculosis patients became laboratory or x-ray technologists. Five of the 15 amputee clients were trained as prosthetists. In all occupational categories there seemed to be a good matching of professional job demands with the physical capacities of the trainees.

The numbers of clients by disability category were studied, and it was found that the proportion of those who had had tuberculosis and who became clinical, laboratory, or x-ray technologists was considerably greater than, and statistically significantly different (chi square analysis [8]) from, those who entered the same occupational category from the groups poliomyelitis residua, bone and joint disorders, visual defects, and amputations.

The spectrum of disabilities encountered in this group is somewhat disproportionate to the case load seen in most rehabilitation centers. No clients with paraplegia or hemiplegia were seen here, and the number of clients with healed pulmonary tuberculosis is high. This is understandable, however, for the placement of these former patients in industry is difficult, since, apparently, some employers still have prejudicial attitudes toward these persons. Conversations with personnel directors in tuberculosis hospitals have indicated that many who have had tuberculosis have become employees in the institutions where they were patients. Of the amputees, 10 had single amputations of the lower extremity, 3 had double amputations, one had a single upper extremity amputation, and in one client three fingers had been amputated. Among those categorized as having visual defects were several who had had enucleations or unilateral blindness. None was totally blind. Only one individual had a psychiatric disorder (anxiety reaction), and she became a nurse. The bone and joint disorders other than osteomyelitis and postfracture states included arthritis, ankylosed joints, tuberculosis of the femur, and osteochondritis.

TABLE 2.—*Medical and Paramedical Clients Rehabilitated, by Disability and Occupation*

Disability	Clients		Persons by Occupation, No.															
	No.	%	Bacteriologist	Dental Technologist	Dentist	Dietitian	Laboratory Technologist	Medical Social Worker	Nurse	Nurses' Aide	Occupational Therapist	Optician	Optometrist	Pharmacist	Physician	Prosthetist	Practical Nurse	X-ray Technologist
Totals	190	100.1	4	18	9	6	35	1	26	11	1	1	3	11	17	7	26	14
Tuberculosis, pulmonary, stable	42	22.1	1				16	1	3	2	1				4		4	10
Poliomyelitis residua	25	13.2		5	2	1	6		5					1	5			
Bone and joint disorder, miscellaneous	20	10.5	1	3	2	1	2		3	1				3	2		2	
Visual defect	16	8.4		1	1				2	3			1	2	1		5	
Amputation	15	7.9		3	1										1	5	2	3
Fracture, malunion	8	4.2					1		2					1	1		3	
Hearing defect	8	4.2	1	1		2	1		1								2	
Osteomyelitis, chronic or well	8	4.2			2		1		1			1	1			2		
Congenital anomaly	6	3.2		1			1		1					1	1		1	
Dislocation of hip, congenital	5	2.6			1	1			2	1								
Convulsive disorder	4	2.1					1			2							1	
Heart disease	4	2.1					1		1						1		1	
Spastic paralysis	4	2.1					1			2				1				
Speech impairment	4	2.1	1	2			1											
Deformity, post-trauma, etc.	3	1.6					2							1				
Pulmonary disorder, miscellaneous	3	1.6							1				1		1			
Disfigurement of face	2	1.1							2									
Diabetes mellitus	2	1.1				1												1
Hernia	2	1.1															2	
Peptic ulceration	2	1.1												1			1	
Varicose veins	2	1.1							1								1	
Albuminuria, orthostatic	1	0.5					1											
Anxiety reaction	1	0.5															1	
Brucellosis, chronic	1	0.5		1														
Burn residua	1	0.5							1									
Hypertension	1	0.5		1														

Cost of Rehabilitation

Expenditures made in the total rehabilitative process are concerned with such costs as training, physical examinations, prostheses, physicians' fees, maintenance, and supplies. (Physical examinations are conducted by different physicians from those performing the corrective surgery or carrying out specific modalities of care. Hence, this cost item is considered separately, even though the examinations are conducted by physicians and do represent physicians' fees.) In table 3 are seen the total costs per year for all clients in the categories considered here. The over-all cost for the 190 clients was $95,470 and averaged $533 per person rehabilitated, with a range from no cost to $5,282. (Eleven of the clients received services representing no direct costs, such as counseling, placement, or evaluation. The lowest direct expenditure for a rehabilitee was $2 for a cane.) The average cost of training was $466; the average physicians' fee, $47; the average cost of physical examination, $4; the average cost of prosthesis, $130; the average cost of maintenance, $416; the average cost of supplies, $231; and the average of other costs, $151. The greatest expenditures were for training ($62,881) and maintenance ($21,653). Training included where appropriate, the sponsoring tially or totally through medical, nursing, dental, or pharmacy school. If the client is deemed eligible in light of his potential, his age, his financial need, and his disability, he or the agency concerned will be given the funds necessary for the education. Fortunately, the supporting source of individual clients is not known to their classmates, and several of the physicians of the group were trained at the University of Oklahoma School of Medicine, without the DVR's relationship becoming common knowledge. The top figure of $5,282 was aid for one of the physicians who had undergone rehabilitation. For approximately $95,500, therefore, 190 medical professional or semiprofessional persons had been added to a tight labor market.

Table 3.—*Costs of Rehabilitation of All Medical and Paramedical Clients per Year by Category of Cost*

Yr.	Training, $	Physicians' Fees, $	Physical Examinations, $	Prostheses, $	Maintenance, $	Supplies, $	Other Costs, $	Total Costs, $
1937-1938	2,446		107	45			138	2,736
1938-1939	2,531		25					2,556
1939-1940	165			102				267
1940-1941	1,540				120	1,112		2,772
1941-1942	998				530	45		1,573
1942-1943	1,805	65		903				2,773
1943-1944	...	...	...	...	...	...	...	...
1944-1945	1,582			612	365			2,559
1945-1946	2,281	20	5	125	879			3,310
1946-1947	1,684	10		15	1,603			3,312
1947-1948	2,476	75	15	140	242		492	3,440
1948-1949	2,048	28	28		450			2,554
1949-1950	7,240	75	42	527	5,956			13,840
1950-1951	4,787	57	28	153	169		341	5,535
1951-1952	991		56	14	1,057		69	2,187
1952-1953	4,138	182	45	96	3,477		1,096	9,034
1953-1954	3,467	360		1,049	1,712		1,356	7,944
1954-1955	4,613	100		269	1,410		106	6,528
1955-1956	9,268	130		131	2,828		165	12,822
1956-1957	8,791	72			855		10	9,728
Totals	62,881	1,174	351	4,181	21,653	1,157	4,073	95,470

Return of Investment

If one were to consider the advantages accruing from the rehabilitation of these 190 persons, there would be many: the restoration of human dignity through the creation of productive citizens, the development of needed occupational skills, and, through this provision of training, the obviating of the individual's need for public assistance for himself or his dependents at a period in life when manual or unskilled labor is no longer possible. These are a few of the visible benefits; many are the intangible values as well.

To measure the process in terms of money alone, one may compare the costs of rehabilitation with the potential return to the governments whose agencies have expended funds to develop these 190 persons. If we use the figure of 65 years as the point of retirement—although in some instances of self-employed professional persons this falls short of the actual work life—one finds that about 5,643 man-years of productive effort will ensue. To be sure, some of the clients may marry and become housewives, others will change job categories, some will become ill for varying periods, and a few will die prior to the 65th birthday. But, lacking this information, we assume that a work span from date of completion of rehabilitation services to age 65 will be utilized.

Table 4 points up the amounts returned or to be returned to the federal and state governments by this group of 190 during the periods of their practice or work, in the form of taxes, on $34,224,012 of income. (In computing the income tax, a consistent estimated average figure was used for number of dependents for all clients.) It will be seen that $5,598,638 is the anticipated federal tax return, and to the state government, $179,425—a total of $5,778,063, or a return on the investment of over sixtyfold. In any economy, this would be considered a blue chip. For each $533 average cost per client for rehabilitation, there is $30,410 returned in income taxes during the work life of each of these medical or paramedical rehabilitees.

Comment

In an effort to demonstrate that vocational rehabilitation produces personnel other than craft, custodial, or service workers, the 20-year experience of the Oklahoma State Division of Vocational Rehabilitation was reviewed to identify medical and paramedical personnel who were rehabilitated. Of all clients rendered service in those 20 years, there were 190 rehabilitated persons who were trained for and engaged in practice or work in one or another of the medical professions or paramedical activities. Of 16 occupational categories into which

Table 4.—*Income Taxes Returned or to Be Returned by Rehabilitated Medical and Paramedical Personnel During Work Lives*

Occupation	No.	Range of Age When Rehabilitation Service Completed, Yr.	Anticipated Income of Total Group During Work Life to Age 65, $	Total Amount of Federal Income Tax Paid and to Be Paid Prior to Age 65, $	Total Amount of State Income Tax Paid and to Be Paid Prior to Age 65, $
Bacteriologist..	4	26-40	588,000	160,800	1,526
Dental technologist.......	18	18-54	1,525,100	233,216	879
Dentist..........	9	24-35	4,088,194	617,232	39,478
Dietitian........	6	22-28	1,061,402	183,000	2,659
Laboratory technologist...	35	18-44	4,478,100	733,320	8,278
Medical social worker........	1	38	121,500	21,060	321
Nurse............	26	20-45	3,718,800	619,800	7,950
Nurses aide......	11	18-64	627,320	81,384	...
Occupational therapist......	1	36	101,400	17,100	223
Optician.........	1	22	219,300	38,400	718
Optometrist.....	3	25-39	1,028,970	203,734	8,219
Pharmacist.....	11	21-49	2,182,800	385,200	7,147
Physician.......	17	21-29	10,903,946	1,804,976	97,585
Prosthetist......	7	19-56	1,162,800	205,200	3,708
Practical nurse..	26	19-61	1,124,040	158,688	...
X-ray technologist...	14	20-38	1,289,040	191,928	734
Total...........	190		34,224,012	5,598,638	179,425

the clients were placed through professional training, the following led numerically: nurses (professional and practical) 52, laboratory technologists 35, dental technologists 18, physicians 17, and x-ray technicians 14.

There were 26 different disabilities represented by the rehabilitees, the greatest number being stable pulmonary tuberculosis (22.1%), with poliomyelitis residua second (13.2%), bone and joint disorders third (10.5%), and visual defects fourth (8.4%). Of the former tuberculosis patients, 62% became laboratory or x-ray technologists.

The over-all cost for rehabilitating the 190 clients was $95,470, which averaged $533 per person, with a range from no cost to $5,282. Expenditures were made for training, physical examinations, prosthetic fees, physicians' fees, maintenance, and supplies. Not all clients represented direct costs, for in 11 cases services were received with no attached cost apart from overhead.

Some of the benefits accruing from rehabilitation of a professional group may be seen in the restoration of human dignity, the development of needed occupational skills, and the precluding of the need for public assistance at a period in life when unskilled labor is no longer possible. To measure the worth of the rehabilitation process in money alone, the anticipated work-life income has been calculated and the federal and state income taxes accruing from this income extrapolated from the date of termination of rehabilitation to age 65. The 190 persons would earn $34,224,012 in 5,643 man-work-years. From this income there would accrue to the federal government in income taxes the sum of $5,598,638 and to the state government in income taxes $179,425, representing a return on the rehabilitation investment of over sixtyfold. For each $533 average cost per client for rehabilitation, there is returned in income taxes $30,410 during the work life of each of the medical or paramedical rehabilitees.

Conclusions

Through the federal-state vocational rehabilitation program, professional persons have been trained for entry into the medical and paramedical professions. The investment of tax funds in the rehabilitation of professional persons is sound in view of the development of productive citizens in needed occupational categories, the restoration of human dignity, and the lowering of public assistance grants. The sixtyfold return on the investment in rehabilitation bespeaks the wisdom of rendering aid to those persons capable of undertaking professional curriculums.

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Grateful appreciation is expressed to Mr. Robert G. Davis, Mrs. Barbara Kirby, and Mrs. Bobbie Hurt (Department of Preventive Medicine and Public Health [Occupational Medicine]) for the compilation of the data, to Mrs. Ruby Creech, Mrs. Mary Thompson, and Miss Maude Goss, of the State Division of Vocational Rehabilitation, for the extraction of the basic data, and to Mr. Voyle C. Scurlock, Director of the State Division of Vocational Rehabilitation, for his cooperation in this study.

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ABSTRACTING MACHINE.—Scientists struggling with the flood of technical literature may soon get some mechanized assistance. H. P. Luhn of the International Business Machines Corporation has programmed a 704 computer to "read" articles (on punch cards) and to click out a crisp summary of their contents. The summary, which Luhn believes is as good as or better than a man-made abstract, consists of a few of the most significant sentences from the article, quoted in their entirety. To weigh significance the machine lists every word used in the text and counts the number of times each appears. Discarding trivial words such as "the" and "and," the automatic abstracter prepares a table of the most-used words. It then scans each sentence and picks out the ones that contain the greatest concentrations of these words. The highest-scoring sentences are printed as the abstract. Luhn points out that one advantage of the machine is that it judges significance objectively, not from the prejudiced point of view of a specialist. What its abstracts "lack in sophistication, they will more than make up for by their uniformity of derivation."—Science and the Citizen, *Scientific American*, June, 1958.

EFFECT OF RELAXIN ON NORMAL LABOR

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Two preparations of relaxin, a water-soluble substance extracted from the bovine corpus luteum, were compared with a placebo in a series of 47 obstetric patients. The series included 24 primiparas and 23 multiparas. These were distributed among the three groups who received, respectively, relaxin A, relaxin B, and the placebo. The placebo, like the relaxin preparations, was given in diluted form by slow venoclysis. The three groups were compared as to duration of labor, degree of softening of the cervix, and other possible signs of an effect of the relaxin preparations on the course of delivery. No significant differences were found.

In 1926 a water-soluble extract of the corpus luteum of sows was found to contain a principle able to produce relaxation of the ligamentous structures of the pelvis of the castrated guinea pig.[1] The discoverer and his associates, after further laboratory investigation, adequately confirmed its existence in other animals and in the human and were able to demonstrate that it could be recovered in higher concentrations in the corpus luteum during pregnancy.[2]

Early investigations were carried out in the experimental animal, and most of the effects produced by this hormone were regarded only as interesting physiological phenomena. Early in 1955 the first report was made of its beneficial effect in forestalling the onset of premature labor,[3] and in the succeeding two years confirmation was to be had with highly purified commercial preparations of known potency.[4]

On the basis of a previous experiment carried out in the sow [5] that demonstrated a definite ability of relaxin to soften and dilate the cervix prior to the onset of labor, experiments were set up to determine its effectiveness in the human.[6] Shortly after that it was reported that the hormone was of value in reducing the length of labor [7] and in facilitating dilatation of the cervix. Our own results in tests with relaxin had been equivocal,[6] and in our opinion favorable reports were rendered impossible of interpretation by a failure to use untreated controls and by combining the unknown drug with a substance of known but unpredictable action (oxytocin).[7] In order to reevaluate our own pilot series and to appraise more thoroughly a substance which could have such potential value, a double-blind experiment was designed to investigate the effect of relaxin alone on the normal term gravida in labor.

Materials and Methods

From July, 1957, to February, 1958, we treated 47 patients with two commercial preparations of relaxin and one preparation of an inactive solvent. The patients were taken from the private practice of one of us and the clinic clientele of the other. They were unselected save for the following criteria: 1. There could be no medical or obstetric factors complicating the antenatal course or delivery. 2. The patient would have entered the hospital before the cervix had progressed to 5 cm. in dilatation. 3. The vertex would be presenting. 4. Engagement must be approximated.

When the observer was assured of progressive cervical dilatation and the os was opened not less than 3 and not more than 5 cm., the contents of a bottle containing 2 cc. of a liquid were diluted to 250 or 500 cc. with 5% glucose or normal saline solution, and intravenous injection was begun at such a rate that the contents would be exhausted in from 45 minutes to 1½ hours. The contents of the bottles were known to the examiner as a number and to the patient only as a "new substance that is designed to ease labor and cause the mouth of the womb to open with less difficulty."

The two commercial preparations of relaxin, of known potency, were utilized and were designated "A" (Releasin) and "B" (Cervilaxin). The third vial, labeled "C," was a control solution of solvent which appeared no different from the active preparation in packaging, viscosity, or color. The consistency of the cervix was determined at the onset of the experiment by sterile vaginal examination, which also confirmed the degree of dilatation and consistency of the cervix. Consistency of the cervical tissue that was similar to that of the lip was considered 1+, while a hardness that approximated the feel of the tip of the nose was considered 4+. Intermediate stages were labeled 3+ and 2+ according to the individual examiner's judg-

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ment. After the infusion of the drug the sterile vaginal examination was repeated and the consistency reevaluated.

For the purposes of the experiment the onset of labor was said to have started not when contractions became progressive and/or regular but when cervical dilatation was known to have started and to have become progressive. Time was stopped at full dilatation. The projected course of cervical dilatation was estimated and placed on the chart, along with the estimated time of delivery, as the medication was started. For charting purposes the time of estimated labor was divided into quarters, and progress was graphed, with cervical dilatation as the ordinate and time in hours as the abscissa.

Medication for the relief of discomfort was given without regard for cervical dilatation or for the point of usage of the relaxing factor. Most of the patients had parenteral medication of moderate dosages of meperidine (Demerol) hydrochloride, and an adjuvant such as scopolamine hydrobromide, promazine (Sparine) hydrochloride, promethazine (Phenergan) hydrochloride, or a barbiturate. A few were rendered comfortable and delivered with the use of block anesthesia. Rarely amniotomy was utilized, and when it was thought necessary it was carried out well in advance of the infusion of the experimental material or well after the infusion was terminated.

Table 1.—*Comparison of Labor Time in Experimental and Control Groups*

	Primiparas		Multiparas	
	Patients, No.	Length of Labor, Hr.	Patients, No.	Length of Labor, Hr.
Relaxin (A)	9	9.2	7	5.0
Relaxin (B)	8	8.7	7	4.7
Total	17	9.0	14	4.9
Controls	7	9.0	9	4.2

After delivery, the actual time of delivery was charted and the curve of cervical progress completed for comparison with the estimated curve and prognosticated time of delivery. At the termination of the total experiment the number of each bottle was compared with the key and catalogued as to the type of material that it contained. It was found that the control material had been utilized on seven patients with the first pregnancy and on nine who were having the second or more. Seventeen of the primiparas and 14 multiparas had been given active medication (relaxin). The division between the two commercial preparations had been 16 for product A and 15 for product B.

Results

Of the 24 primiparas who received medication 17, or 61%, received relaxin and 7, or 29%, were given the placebo. The total length of progressive labor was smoothed off to average slightly less than nine hours in the experimental series and nine hours in those who received inactive material (table 1).

Fourteen multiparous patients (60%) received relaxin, and nine (40%) were given the placebo. The total length of observed labor in this group averaged less than five hours. It was slightly less although not significantly so in the control group—4.2 hours as against 4.9 hours in the experimental group (table 1).

Table 2.—*Degree of Softening of Cervix, During Experimental Periods, of Experimental Group and of Control Group*

	Primiparas		Multiparas	
	Patients, No.	Degree of Softening, %	Patients, No.	Degree of Softening, %
Relaxin (A)	9	5	7	25
Relaxin (B)	8	12	7	10
Total	17	8	14	17
Controls	7	17	9	10

In the primipara during the hour and a half of medication, the cervix was found to be softened approximately 8% in the experimental group and 17% in the control group (table 2). Softening of the cervix during this time in the multipara was estimated at around 17% in the experimental group and was found to vary insignificantly with the controls, in which it changed 10% (table 2). In the primipara (fig. 1, *top*) the calculated curve of the progress of labor closely accompanies the estimated one, and the time of prognosticated length of labor approximates the actual time (when both figures are smoothed to the closest number).

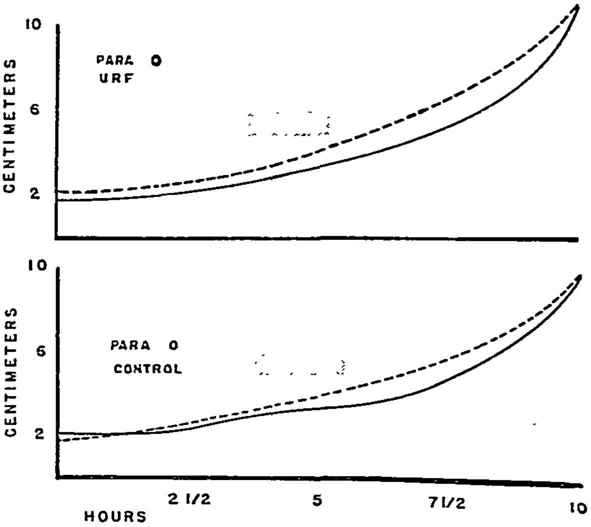

Fig. 1.—*Top*, calculated and estimated rates of cervical dilatation in primiparous patients who were given relaxin. Solid line shows observed rate, and interrupted line shows expected rate; crosshatching shows mean time during which medicament was infused. *Bottom*, observed and estimated rates of cervical opening for primiparous patients who received placebo. Not only do the estimated and observed rates closely follow each other but there is little difference in rate between patients given relaxin and the control groups.

Figure 1, *bottom*, gives a graphic picture of the estimated and calculated curve of cervical dilatation of those primiparas in whom the placebo was employed. Here too the time of labor is seen to coincide with the estimated course in both the experimental groups. In the multiparous groups, too, the estimated course of dilatation of the cervix closely followed the calculated curve in both the experimental and control groups (fig. 2).

Comment

The difficulty is recognized of evaluating any drug or procedure that has as *its end the alteration* of so complex and variable a function as the dilatation of the cervix. In the absence of an impractically *sized sample in* each group the length of labor itself is merely a rough measure; the estimation of individual labor is no more than grossly usable; and even the degree of softening of the cervix is subject to *individual interpretation*. However, these criteria are the best we could follow.

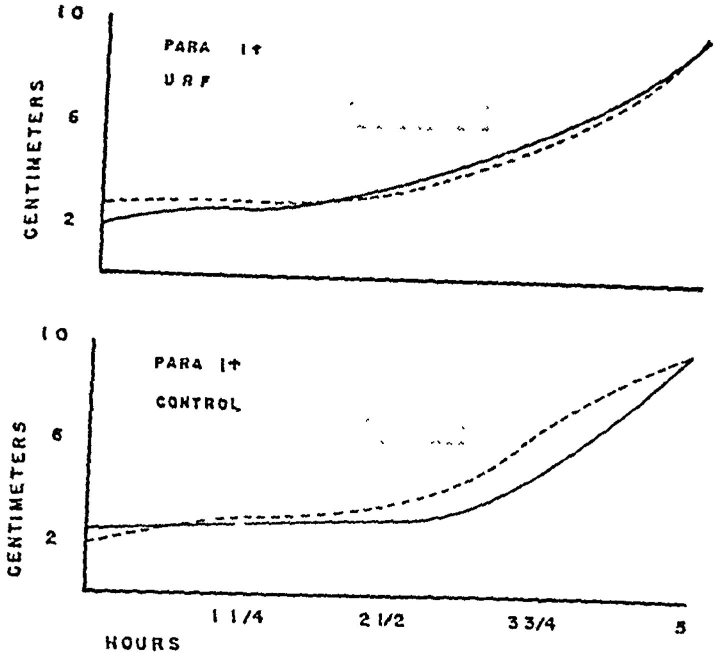

Fig. 2.—*Top*, estimated and observed rates of cervical dilatation for the multiparous patients who received relaxin. *Bottom*, estimated and calculated rate of cervical opening in control patients, showing no significant variation. On comparison with the top figure, it will be seen that the time of dilatation and the characteristic curve are not altered.

In the calculation of the total length of labor the onset was reckoned only after cervical dilatation had begun. Curves of estimated and observed cervical dilatation were smoothed. In calculating the averages, we took the nearest whole figure for the length of labor and diameter of cervix, rather than include fractional numbers. All these methods of simplification are not without objection, but for such a clear-cut experiment refinements of calculation seemed profitless.

In several instances two to three times the prescribed dosages of relaxin have been used in patients with extremely hard cervices, prolonged labors, and uterine dyskinesia to see if we could find a specific effect. Results have not been included in the above data, but no real effect has been recognized in any instance on either the degree of dilatation or change in consistency of the cervical tissue.

In such a multiphasic process as labor the isolation of any one portion (such as the effect of a drug on cervical softening) is not without possibility of error. We have had no method of determining the effect of the drug on uterine forces as labor progresses, and it is not inconceivable that its amelioration of uterine contractions could negate any effect that it might have in facilitating cervical opening. It is of interest, however, that experiments carried out to determine the effect of relaxin in the forces of labor have not shown any consistent effect on uterine contractions in the patient in active labor.[8]

Conclusions

Relaxin has been used on 47 patients in a double-blind experiment in an effort to evaluate its ability to cause increased softening of the cervix and to facilitate cervical dilatation in the course of normal labor. Within the limits of the designed experiment it has not been possible to demonstrate its value.

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TREATMENT OF ACUTE LEUKEMIA IN CHILDREN AND ADULTS

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Acute leukemia was treated in 46 children and 29 adults by five different therapeutic regimens. The largest group, consisting of 55 patients, received steroids (cortisone or prednisone) with 6-mercaptopurine; 9 received 6-mercaptopurine only, 5 received steroids only, and 6 received other forms of treatment. The remission rate for all the children treated was 77%; some went on to a second remission, and one went to a third. The rate of remissions for adults was only 17%, and there were no second remissions in any of the adult patients. The data on survival times proved difficult to compare. The duration of life was nearly the same in each group, as was the duration of therapy needed to induce remission. The duration of remission appeared to be longest in those patients who received a combination of 6-mercaptopurine and steroids, but the limited size of the other groups made comparison difficult. The steroid treatment caused a noticeable weight gain and some other undesired effects but no electrolyte imbalance, hypertension, or peptic ulcer. The undesired effect of 6-mercaptopurine was occasional, sudden, excessive leukopenia. The 50% survival time in the group who received 6-mercaptopurine was 9 months, and the 10% survival time was 19 months.

The introduction of the folic acid antagonists for the treatment of acute leukemia has opened a new era of hope for the leukemic patient. Not only has the prolonged survival time been symptom-free, but the effective use of metabolic blocking agents in acute leukemia was realized. Many new compounds have been and will be synthesized, yet only a fraction will filter through the maze of laboratory and clinical screening to become therapeutically useful. Since the incidence of leukemia is small, evaluation of newer agents has been a slow and empirical process. Accurate evaluation of newer agents requires comparison of their effects to those of known agents. Simultaneous comparisons, with random selection of patients, appear to be the most reliable method of analysis in order to minimize bias, account for changes in the natural course of the disease, and develop newer, more effective supportive measures. Only recently have such studies been possible through the cooperative participation of several institutions pooling their resources. The purpose of this report is to relate our experience in treating 75 patients with acute leukemia, primarily with simultaneous use of combinations of steroids and 6-mercaptopurine.

Methods

All patients with acute leukemia entering the clinic for treatment during the past four years were placed on therapy with combinations of steroids (cortisone, prednisone, or ACTH) and 6-mercaptopurine, regardless of age or state of disease. Exceptions were made to those patients who received antileukemic therapy before entering the clinic and to those placed in the acute leukemia cooperative study group. A critical evaluation of the response to therapy takes into account not only the antileukemic agents used but also the supportive care given to the patient. The latter was not uniform in this series since other physicians assumed management of these patients on some occasions. Our preferred details of care, including use of antibiotics only when indicated, no vitamins, and energetic investigation for complications accompanying acute leukemia were not always possible. In those patients with severe thrombocytopenia, platelet transfusions were not utilized in efforts to forestall the onset of fatal hemorrhage.

Dosage.—6-Mercaptopurine was used in the standard recommended dosage of 1 to 2 mg. per pound per day. Cortisone dosage varied in children from 100 to 200 mg. per day and in adults from 200 to 300 mg. per day. Prednisone dosage in children ranged from 40 to 60 mg. per day and in adults from 60 to 100 mg. per day.

The initial dosage of steroids was maintained until a no apparent disease state was achieved. (The term "no apparent disease state" is used to denote the absence of leukemia by hematological and clinical examination at the time of observation, as defined by the criterion devised by the acute leukemia cooperative study group. Once this state is achieved and maintained the patient is then considered to have achieved a complete remission.) This dosage was then gradually decreased to main-

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tenance levels sufficient to maintain the desired state of the disease without toxic side-effects. In 13 children who attained remission, the average maintenance dose of cortisone was 66 mg. per day (the range was 12.5 to 100 mg. per day), and in 3 receiving prednisone maintenance doses ranged from 10 to 20 mg. per day. During remission the dosage of 6-mercaptopurine was reduced to levels of 0.3 to 0.7 mg. per kilogram per day. The maintenance steroid dose in adults was 50 to 100 mg. per day in three patients receiving cortisone and 15 to 20 mg. per day in two patients receiving prednisone. The maintenance dose of 6-mercaptopurine ranged from 50 to 100 mg. per day.

The initial dosage of 6-mercaptopurine and steroids was maintained throughout the course of the disease in those patients not achieving a remission. The dosage of 6-mercaptopurine in adults was 50 to 500 mg. per day (0.7 to 3 mg. per pound); in addition, 3 received ACTH (20 to 100 mg. per day); 11 received cortisone (75 to 400 mg. per day); and 4 received prednisone (15 to 40 mg. per day). In children 0.2 to 1.3 mg. per pound per day of the 6-mercaptopurine was given in addition to cortisone in six (25 to 75 mg. per day) and prednisone in two (60 to 80 mg. per day).

Return visits to the outpatient clinic were at weekly intervals until a no apparent disease state [illegible] achieved, after which return visits were re- of simplification [illegible]-four-week intervals. During each such a clear-cut exal evaluation consisted of deter- tion seemed profitles.

mining the hemoglobin level, the total white blood cell count, and the differential count of the blood. Other hematological tests were performed whenever indicated. Bone marrow examinations were performed initially and whenever the disease state was in question. Classification of the disease state was based on peripheral blood, physical features, and clinical features and did not include bone marrow evaluations. The criteria used in evaluating these features were those revised by the acute leukemia cooperative study group.[1]

Results

There were 75 patients: 46 children (19 female and 27 male) and 29 adults (15 female and 14 male). Five regimens were used: 1. Fifty-five patients received steroids with 6-mercaptopurine. 2. Five patients received steroids with folic acid antagonists. 3. Five received only steroids. 4. Nine were given only 6-mercaptopurine. 5. One child received 6-mercaptopurine with 6-diazo-5-oxo-L-norleucine (DON). A summary of patients is given in the table.

6-Mercaptopurine–Steroid Group. – Thirty-two children and 23 adults were treated with a combination of 6-mercaptopurine and steroids.

Children: Of the 32 children treated, 6 were lost in follow-up. A no apparent disease status occurred in 16 out of 21 (76%) patients less than 15 years of age.

TABLE 1.—*Summary of Data on Patients with Acute Leukemia Treated with Different Antileukemic Regimens*

	Patients, No.		Age, Yr.		Onset of Symptoms to Onset of Therapy, Wk.		Onset of Therapy to Beginning of Remission, Wk.		Duration of Remission, Wk.		Remission, %	End of Remission to Death, Wk.		Duration of Life, Wk.		Duration of Treatment, Wk.	
	Total	Males	Range	Mean	Range	Mean	Range	Mean	Range	Mean		Range	Mean	Range	Mean	Range	Mean
Steroids + 6-mercaptopurine																	
Children																	
Remission																	
< 15	16	11	2.5-15	6.5	0.7-21	5.27	2-14	5.4	2-68	20.1	76	0-28.3	10.6	21-91	44.9	15.1-77.1	37.8
> 15	3	1	17-19	18.3	6.4-21.3	9.2	3-5.4	4.5	3-28	9.0	60	5.4-14.6	10	24-44.1	37.4	19-38	26.6
No remission																	
< 15	5	2	0.25-11	8	0.3-11	1.5	...	...	...	...	24	...	...	2-15.4	7.0	1.6-13.4	6 5
> 15	2	1	17-19	18	2.5-32	...	...	...	...	...	40	...	...	5.7-54.0	...	3.2-28	...
Unknown outcome	6	3	2.5-15	...	...	...	...	...	...	...	18.8	...	...	...	...	...	...
Adults																	
Remission	5	3	33 66	36.3	4-12	8.2	2.9-10.0	4.9	4-23.9	12.3	22.6	2-15	9.04	17.3-49.2	34.6	11.4-37.2	26.7
No remission	17	7	20-66	41.1	2-31.4	11.4	...	...	...	...	77.4	...	...	5-36.7	17.4	0.7-29.3	6.7
Unknown outcome	1	1	33	...	12	...	...	...	...	...	4.3	...	...	...	...	...	...
Steroids + antifolic acids	5	4	1.5-8	7 7	2-24.0	9.8	2-10	5.3	2-35	13.1	100	5-16.9	10.9	21.3-98.0	46.4	21.6-74.0	41.5
Steroids only																	
Children	3	1	2.5-9.0	...	1	...	3.3-2.9	...	10-36	...	100	5-15.3	12	44.3-134.3	...	31.9-132	...
Adults	2	2	38-43	...	18.9-24.7	...	...	...	...	...	100	...	...	28.7-32.7	...	4.7-8	...
6-Mercaptopurine only																	
Children																	
Complete remission	1	1	4	...	6	...	3.1	...	4	...	25	14.7	...	27.8	...	21.8	...
Incomplete remission	1	...	6	...	24	...	4.4	...	3	...	25	2.7	...	52	...	10.1	...
No remission																	
Later with antifolic acids	1	...	3	...	4	...	6.3	...	7.6	...	25	24.4	...	42.3	...	38.3	...
Never	1	...	3	...	7.6	...	...	...	...	...	25	...	...	...	10.2	...	2.6
Unknown outcome	1	...	3	...	6.0	...	...	...	...	...	20	...	...	...	...	...	...
Adults—No remission	4	1	28-72	48.7	4.6-21	10.1	...	...	...	...	100	...	...	1.25-21.7	9.4	0.7-2	1 3
6-Mercaptopurine + DON	1	...	5	...	18	...	8.6	...	8.9	...	...	16.5	...	52	...	34	...

The duration from onset of therapy to onset of complete remission ranged from 2 to 14 weeks (mean, 5.4 weeks; median, 4 weeks; 95% limits, 1.4 to 9.2 weeks). (The median was taken as the 50% survival intersect of the best visual linear regression of cumulative survival data plotted on log-probability paper; 95% limits were taken as the ±2 probit intersects of the same line.)[2] Complete remission was maintained from 2 to 68 weeks (mean, 20.1 weeks; median, 14.0 weeks; 95% limits, 3.1 to 66.0 weeks). During remission patients were completely asymptomatic and were able to attend school and to participate in normal recreational activities. Initial hemoglobin levels ranged from 2.4 to 13.5 Gm. per 100 ml. Twelve patients had anemia, two requiring transfusions. During remission hemoglobin levels ranged from 11.7 to 14.7 Gm. per 100 ml. (mean, 13.3 Gm. per 100 ml.). Initial white blood cell counts ranged from 7,000 to 176,800 cells per cubic millimeter (three with less han 2,000, five with more than 15,000). During complete remission leukocyte counts ranged from 4,200 to 12,000 cells per cubic millimeter (mean, 5,800 cells per cubic millimeter). The total circulating granulocytes initially ranged from 0 to 3,000 cells per cubic millimeter (3 with more than ,500 cells per cubic millimeter) and during remission ranged from 1,800 to 8,400 cells per cubic millimeter (mean, 3,200 cells per cubic millimeter). The segmented neutrophils predominated he peripheral blood during remission (range from 47.74 to 74%. No blast cells were observed in the peripheral blood during remission. In all patients he rapid appearance of blast cells in the peripheral blood heralded the onset of relapse. In two a concomitant reduction in hemoglobin level also occurred. Treatment was usually altered after regression (relapse) from a no apparent disease state. Six patients remained on the combination 6-mercaptopurine–steroid regimen throughout the entire course of their illness. One attained a no apparent disease state for the second time which lasted seven weeks. Three other patients who remained on herapy with the 6-mercaptopurine–steroid combination received in addition folic acid antagonists. A moderate disease state was induced in one paient. One of two patients who received a combinaion of aminopterin and steroids achieved a second complete remission. A second remission occurred in one of two patients given aminopterin. Another patient received 6-mercaptopurine without effect. Two patients died while in a no apparent disease tate. The reasons for these deaths could not be explained at autopsy. Three patients died from massive hemorrhage, eight from overwhelming inection, two from central nervous system complicaions, and one from unknown causes.

The duration of life from onset of symptoms to death ranged from 21 to 91.2 weeks (mean, 44.9 weeks; median, 35 weeks; 95% limits, 15 to 80 weeks). Duration of treatment from onset of treatment to death ranged from 15 to 77 weeks (mean, 37.8 weeks; median, 32.2 weeks; 95% limits, 10.4 to 100 weeks).

In three patients between the ages of 15 and 20 years a no apparent disease state was obtained 3, 5, and 5.4 weeks after the onset of treatment. This state was maintained for periods of 3, 5, and 28 weeks. All of these patients died from septicemia 5.4, 10, and 14.6 weeks after the end of the no apparent disease state. Only one remission was seen, and one regimen was used throughout the entire course of the disease.

Therapy with a combination of 6-mercaptopurine and steroids failed to induce a no apparent disease state in seven patients. Five were treated for less than two weeks, which did not appear to be a sufficient interval for the effect of the agents to become manifest. All of these patients died from fatal hemorrhage. If these are eliminated, the remission rate for this combination would be 19 out of 21 patients (90%) for the 0-to-20-year-old group. The leukemic state in the other two patients did not appreciably change for 13 and 28 weeks respectively. One eventually died from a massive hemorrhage and the other from Pseudomonas aeruginosa septicemia. Initial hemoglobin levels were less than 10 Gm. per 100 ml. in four patients. All patients had profound anemia at the time of death. Leukocyte counts ranged initially from 9,800 to 180,000 cells per cubic millimeter (4 with more than 15,000 per cubic millimeter); the majority of the patients had elevated leukocyte counts. The interval between the onset of symptoms and the onset of treatment ranged from 0.3 to 32 weeks (mean, 6.3 weeks) in the patients with no remission and 0.7 to 21 weeks (mean, 5.3 weeks) in patients attaining remission.

Adults: In the adult group a no apparent disease rating was achieved in 5 out of 23 (22% remission rate) patients with leukemia 20 years of age or older. Complete remissions occurred during the 3rd week of therapy in three and during the 5th week and 10th week in the other two patients. Complete remission was maintained for 4 to 24 weeks. This state was achieved only once in each patient. Combinations of steroids and 6-mercaptopurine were the only agents used during the entire course of the disease. The average duration of therapy was 26.7 weeks (range, 11.4 to 37.2 weeks), and the duration of life from the onset of symptoms ranged from 17.3 to 49.2 weeks (mean, 34.6 weeks). Three patients died from septicemia, one from intracranial hemorrhage, and the other from undetermined causes.

In 18 patients no effect from the combination of 6-mercaptopurine and steroids could be seen. The outcome of one patient is unknown. Nine were on therapy with the combination for four weeks or less, five between 4.1 and 6 weeks, and three for 8.9, 11.0, and 29.3 weeks. During the first month of therapy four patients died from fatal hemorrhage, three from infection, one from renal failure, and one from unknown cause. Hemorrhage and infection accounted for an equal number of deaths in the remaining patients surviving longer than four weeks of therapy. Steroids and 6-mercaptopurine were the only agents used in the treatment in this group. Patients attaining complete remission lived twice as long (mean, 34.6 weeks) as those who failed (mean, 17.4 weeks). The interval between onset of symptoms to onset of treatment was 8.2 weeks (range, 4 to 12 weeks) in the patients attaining a remission and 11.4 weeks (range, 2 to 31.4 weeks) in those who did not develop a remission. The remaining groups were too small for a valid statistical study and are, therefore, described for crude comparison.

Aminopterin-Steroid Group.—All five patients treated with a combination of aminopterin and steroids were children, with ages ranging from 1.5 to 8 years; four were males. Remission occurred in four after 2 to 10 weeks of therapy and was maintained for 2 to 35 weeks. Duration of life in this group ranged from 21.3 to 98.0 weeks. The time from onset of symptoms to beginning of treatment ranged from 2 to 24 weeks. Four patients attained a complete remission. The fifth patient developed a remission after a second course of therapy with a combination of 6-mercaptopurine and cortisone. A second remission (six and nine weeks in duration) occurred in two out of four patients who were given a combination of 6-mercaptopurine and steroids. Three patients died from septicemia, two from massive hemorrhage, and one from a combination of intracranial hemorrhage and bronchopneumonia.

Steroids.—The disease state rapidly regressed in the two adult patients treated with steroids. Both were males, aged 38 and 43. One died from a combination of multiple hemorrhages and bronchopneumonia after 4.7 weeks, and the other died 8 weeks after the onset of therapy from pulmonary infiltration and edema. Three children, aged 2.5, 8.5, and 9 years who were initially treated with only steroids progressed to a no apparent disease state 2.9 and 3.3 weeks after initiation of therapy. Complete remission was maintained for 10, 14, and 36 weeks. A second remission occurred in all three 4, 6, and 26 weeks after termination of the first remission, with use of regimen 1 in two and regimen 4 in one patient. The second no apparent disease state lasted 6, 8, and 37.6 weeks. A third remission of 12.7 weeks duration occurred in one patient 3.3 weeks after termination of the second remission. A combination of aminopterin and ACTH was used. The duration of life was 44.2, 72, and 134.3 weeks. The causes of death were massive hemorrhage, septicemia, and subdural hematoma respectively.

6-Mercaptopurine.—Four adults, aged 28, 39, 56, and 72 died 0.7, 1, 1.7, and 2 weeks after the beginning of 6-mercaptopurine therapy. One died from a coronary infarction and two from massive intracranial hemorrhage. The cause of death was not determined in the fourth patient. Of five children treated (three aged 3, one aged 4, and one aged 6) a moderate disease state occurred in one and a no apparent disease state in two. Remissions were maintained for 3, 4, and 7.6 weeks. Second remissions did not occur despite use of other agents. The duration of life in those with remission was 27.3, 42.3, and 52 weeks and in those without remission 3 and 7.6 weeks. Massive hemorrhage was the cause of death in all except two of the patients undergoing remission. These two died from bronchopneumonia and septicemia.

Comment

The remission rate for all the children treated was 76.9%. If those who died in less than one month after initiation of therapy are eliminated the remission rate is greater, 95%. Nine patients attained either a moderate or no apparent disease state for the second time, after a second course of therapy. In the adult series the remission rate was much less (17%). If those adults who died during the first month of therapy are eliminated, the remission rate is greater, 38.5%. Remissions occurred only in those adults treated with a combination of 6-mercaptopurine and steroids. After relapse subsequent remissions did not occur in any of the adult patients.

Statistical comparison of the effectiveness of the different regimens used in this series would be of little value because of the small number of patients in each group. This is particularly true for the adult patients, since only five were treated with regimens other than combinations of 6-mercaptopurine and steroids. The duration of life appears to be almost equal in each group, being slightly longer in the aminopterin-steroid patients and least in the patients receiving only 6-mercaptopurine. The duration of therapy required for remission was also similar, being slightly longer in those patients given only 6-mercaptopurine and least in those receiving only steroids. The duration of remission appeared longest in those patients who received a combination of 6-mercaptopurine and steroids. The duration of remission was least in the adult patients.

Second remissions were induced in nine children (27.3%), and one achieved a third remission. The duration of life subsequent to the end of remission was similar in all the groups. This was longest in the group who initially received only steroids.

At a casual glance, the remission rate appears higher in this series than those reported by other workers.[3] Patients in this series, however, were classified only on the basis of clinical and peripheral blood findings rather than also on the basis of marrow changes. If bone marrow findings had been evaluated, the remission rate in all likelihood would be similar to those reported by other investigators. The 50% survival time in the 6-mercaptopurine-steroid group was 9 months, and the 10% survival time was 19 months. Burchenal and coworkers[4] reported a 50% survival time of slightly over 12 months in patients receiving sequential therapy of aminopterin, steroids, and 6-mercaptopurine. This difference in survival time may not be entirely accounted for by the difference in method by which antileukemic therapy was used. The mean duration of life was 33 weeks in patients treated prior to 1956 and 52 weeks in those treated after 1956. The 50% survival time in the former group was 28.5 weeks and in the latter 41 weeks. This increased survival time is probably the result of increased experience in use of these agents and more efficient liaison between the hematologist and the attending physicians.

Side-effects from combination therapy were not distressing. Weight gain and Cushingoid changes occurred in all of the patients treated with steroids and, except for cosmetic reasons, were of little significance. No instance of electrolyte imbalance, hypertension, or peptic ulcer occurred. Side-effects from 6-mercaptopurine were also minimal except in those patients who developed sudden reductions in the leukocyte count. This occurred one to two weeks after the onset of therapy. Significant lowering of the white blood cell count occurred in 31 out of 52 patients. These drops in the count ranged from 280,000 to 3,700 white blood cells per cubic millimeter within a two-week period of therapy. In 13 patients the white blood cell count was reduced to less than 2,000 cells per cubic millimeter and in 3 patients to less than 1,000 cells per cubic millimeter. The development of leukopenia posed the problem of differentiating between drug aplasia and leukemic myelophthisis. The inability to aspirate bone marrow in some instances added to the dilemma. Marrow samples could usually be obtained by aspiration from several sites. If spicules were not obtained examination of the sinusoidal blood was often informative. The presence of large numbers of blast cells in the sinusoidal blood was usually regarded as indicating myelophthisis. Myelophthisis, in this series, was found in each instance of leukopenia.

Summary and Conclusions

Seventy-five patients, 46 children and 29 adults, with acute leukemia were treated primarily with a combination of steroids and 6-mercaptopurine. The complete remission rate was 76% but might have been less had bone marrow evaluations been obtained. Side-effects from this combination therapy were minimal.

Leukopenia occurring during 6-mercaptopurine therapy was associated with myelophthisic marrows in this series. This effect was usually seen during the first two weeks of therapy. This may be the result of increased removal of blast cells from the blood, alterations in the release mechanism of the marrow, or temporary initial stimulation of blast proliferation from drug therapy. The remission rate appeared to be higher in the 6-mercaptopurine–steroid group. The 50% survival time, however, was three months less than that reported in other series. Proficiency in the use of these agents and improved supportive care may be the principal factor in the difference. In our opinion the question of the validity of sequential antileukemic therapy versus combined steroid-antimetabolic therapy is not entirely settled and warrants further investigation.

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This study was supported by a grant from the National Cancer Institute of the U. S. Public Health Service.

We wish to acknowledge the cooperation of Dr. William R. Best in preparing the statistical data.

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PROMAZINE, MEPERIDINE, AND SPINAL ANESTHESIA FOR LABOR AND DELIVERY

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Promazine and meperidine in labor afford a method of analgesia and relaxation which appears superior and safer than other modalities in common usage. Ease of administration and minimal side-effects are of particular merit. One hundred consecutive patients were treated with promazine and meperidine followed by spinal anesthesia. The dose of promazine was fixed at 50 mg., given intravenously, for each patient. After medication with promazine, 25 mg. of meperidine was administered intravenously when indicated. Routinely, 50 mg. of meperidine was set as the limit; however, exceptions were made. All patients were given absolute bed rest. Total evaluation showed 57% with excellent results, 29% good, 12% average, and 2% poor. The only patients who should be excluded from the promazine routine are those with a history of asthma. We feel that the nasal and throat congestion may be a reflection of the same processes occurring in the respiratory tree of asthmatics.

In recent times the management of childbirth has developed from the witchery of ancient midwifery to the art of obstetrics, with a steady search for the perfect control of labor and delivery. Major advances in this encyclopedia of medicine have been the development of forceps, antisepsis, and blood banks; and the use of oxytocin (Pitocin), meperidine (Demerol), scopolamine, and antibiotics.

Recently we have used a new technique in the control of labor. This technique was suggested to us by Kuntze and Sison before their article was published.[1] In essence, it is the use of promazine (Sparine) intravenously during labor. Kuntze and Sison and Sprague[2] have employed promazine in labor in conjunction with varied doses of meperidine and scopolamine.

Sprague administered 50 mg. of meperidine, 50 mg. of promazine, and 0.01 mg. of scopolamine intravenously when any analgesia was required in labor. In 86% of his patients he found this procedure to be adequate for excellent analgesia. He used as supplements in the remaining 14% varying doses of the intitial medicaments.

Kuntze and Sison administered 50 mg. of promazine intravenously on admission or when regular contractions were established. This was followed by, or given with, variable doses of meperidine. A small percentage also received scopolamine, atropine, or a barbiturate. In his series, 70% were evaluated as having excellent results.

In both these series the high majority of the patients were delivered under general anesthesia, though a few were delivered with saddle block and only 25 mg. of promazine. Apparently, these authors were concerned with the hypotensive side-effects of both promazine and spinal anesthesia.

In several cases we began to use promazine and meperidine for labor; delivery was accomplished by use of a low spinal anesthesia with 5 mg. of tetracaine (Pontocaine). Our results were so satisfactory that we felt a need for a series of cases to evaluate fully the use of promazine and meperidine in labor followed by spinal anesthesia. No scopolamine is used in our service. We feel amnesia is not a requisite for a properly managed labor. For similar reasons we employ low spinal anesthesia, except where contraindicated.

Initially, we also noted that the use of promazine offered a technique that might easily be standardized for large charity-type hospitals with safety. Therefore, we set out to (1) evaluate the intravenous use of promazine in labor; (2) standardize our procedure; (3) evaluate the side-effects of promazine, especially the hypotensive reaction; and (4) equate these with the best welfare of mother and child in comparison with standard techniques.

Promazine

Promazine, a phenothiazine group drug related to chlorpromazine and promethazine (Phenergan), has many reputed actions and side-effects. The depressive action is particularly on the reticular portion of the nervous tissue. The cortex is not depressed but, rather, the subcortical areas. This drug also depresses the vomiting center. The patient retains full mental capacities, with a relaxing po-

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Read before the Orleans Parish Medical Society Meeting, New Orleans, Feb. 10, 1958.

tential such that the patient appears to be under hypnosis or a quasi-hypnosis such as is used by Read. The potentiating effect of promazine on narcotics has been noted by many workers.

The side-effects of promazine may be divided into minor and major. Under the minor group are allergic skin reactions,[3] generalized pruritus,[3a] dryness and congestion of the nose and throat,[4] constipation,[3a] lethargy,[3] photophobia,[3b] transient blood pressure elevation,[4a] and false-positive frog tests.[5] Under the major group are hypotension,[6] granulocytopenia,[7] convulsions,[8] and jaundice.[9] (In the one case of jaundice reported, the patient also received chlorpromazine.)

Death from promazine therapy has been rare. Of 18 cases of granulocytopenia, 4 ended fatally. In this group, the lowest dose of promazine was 25 mg. given three times a day, and the shortest duration of therapy was 10 days. The average doses were much higher.

The hypotensive effect has been reported as slight and transient, mostly postural in character and easily combated with bed rest or, rarely, with levarterenol. (It has been noted that epinephrine and promazine together have a marked hypotensive effect.) Under this discussion some comment must be made of the marked hypotension noted in patients with an asthmatic syndrome who receive promazine. It has come to our attention from several clinicians[10] that in patients with asthmatic syndromes who received promazine a precipitous hypotensive effect may be noted. This reaction was almost impossible to reverse. This problem has not as yet been fully investigated; however, we believe some awareness of the problem is desirable before detailed studies are made.

Procedure

It was our objective to evaluate 100 consecutive patients treated with promazine and meperidine followed by spinal anesthesia. The dose of promazine was fixed at 50 mg., given intravenously, for each patient. This dose was given when the patient was thought to be in labor but not when the cervix was dilated beyond 4 cm. or when the patient was expected to deliver within three hours. The procedure was soon modified so that all patients were given promazine except when delivery was expected within one hour. Caution was also advised in cases of prematurity, bleeding, and any fetal complication. It was not our feeling that these were absolute contraindications, but with inadequate experience caution must be observed. All patients with a history of asthma were also excluded from the series for reasons given previously.

After medication with promazine, 25 mg. of meperidine was administered intravenously when indicated. Routinely, 50 mg. of meperidine was set as our limit; however, exceptions were made. All patients were given absolute bed rest. From the time of admission through delivery each patient was attended constantly by us or by an intern. At all times we were within minutes of the labor suite for consultation and evaluation. Blood pressure determinations and fetal heart rate studies were made one minute after promazine administration, again in 15 minutes, then 30 minutes, one hour, two hours, the last hour of labor, before spinal anesthesia, and at 5-minute intervals after the spinal injection. During labor the following conditions were also evaluated: patient's response to questions, perineal relaxation, nausea and vomiting, and whether the patient was awake or dozing. The spinal injection of 5 mg. of tetracaine was given with the patient in the horizontal position. The level of anesthesia was then regulated. After delivery the blood loss was estimated. Response of each baby was graded as alert, drowsy, or asleep. The mother was noted to be either awake or asleep after delivery. All stages of labor were calculated, and amnesia, if any, was noted.

Each case was then totally evaluated by the following scale: "excellent" if the patient was relaxed and displayed no evidence of pain or discomfort while in the labor room (32 primiparas and 25 multiparas in our series); "good" when the patient experienced some slight pain or discomfort with contractions near the end of labor (18 primiparas, 11 multiparas); "average" when the patient experienced pain or discomfort with contractions for a significant part of labor (4 primiparas, 8 multiparas); and "poor" when pain and discomfort were noted throughout labor with or between contractions (2 primiparas, no multiparas).

Statistical Results

Our statistics were based on 100 cases handled in the routine outlined above. Fifty-six patients were primiparas. All cases not handled in that manner (i. e., not given promazine because of a history of asthma, not given spinal anesthesia either by choice of the patient or by contraindication, or not given promazine because of lack of time) were eliminated from the series.

Of the study group, total evaluation showed 57% with excellent results, 29% good, 12% average, and 2% poor. In the last two groups, 14 patients were involved. Of the two whose responses were poor, one had a breech delivery (primipara) with promazine given 30 minutes before delivery and the other (primipara) received promazine 9 hours and 11 minutes before delivery. This patient received only 25 mg. of meperidine. Of the 12 with average results, 4 had been given promazine more than 7 hours and 50 minutes before delivery; 1 of these received the drug 18 hours and 30 minutes before delivery. Of the remaining eight, one had a transverse arrest, two had occiput posterior deliveries, one was a markedly neurotic woman, two received promazine less than one hour before delivery, and two had an apparently average labor and delivery.

After administration of the promazine, 59% of the patients had a transient mild blood pressure elevation that reverted to normal in several minutes. From the time of administration of the promazine to immediately prior to the spinal injection, an average depression of 7 mm. Hg systolic and 8 mm. Hg diastolic was noted. The maximum depression was a systolic drop of 40 and diastolic of 30 mm. Hg. The systolic depression occurred in one patient whose blood pressure dropped from 140 to 100 mm. Hg systolic on one occasion one hour after promazine administration; the diastolic drop was from 80 to 50 mm. Hg 30 minutes after promazine was given. There were no other systolic pressures below 90 mm. Hg, nor was there clinical hypotension.

The fetal heart tones were found to be within normal limits in all but one case. At delivery in this case a single coil of umbilical cord was about the infant's neck.

After the spinal injection, the average blood pressure depression was 13 mm. Hg systolic and 9 diastolic. The maximum systolic drop was 40. This patient's blood pressure went from 130 mm. Hg before spinal injection to 90 on two readings after it. The maximum diastolic drop was from 85 to 55, a drop of 30 mm. Hg. Again, there was no clinical hypotension.

The average length of labor was 8 hours and 49 minutes. The average time from promazine administration to delivery was 3 hours and 43 minutes. The minimum was 30 minutes; the maximum was 18 hours and 30 minutes. The average estimated blood loss was 220 cc. The average dose of meperidine was 35 mg. The range was from 0 to 200 mg. During labor 76% of the patients dozed and were relaxed throughout, while 64% slept post partum. Nausea or vomiting occurred in 22%; however, in most cases it was transitory and occurred at full dilatation of the cervix. During labor all the women responded to questions and requests. After delivery 31% showed some amnesia for part or all of the labor.

Eighty-five per cent of the newborn infants were fully alert and had a vigorous cry at delivery; 12% were drowsy. Of this group of 12, 2 were breech deliveries, 2 had an excessive amount of mucus, one had been in fetal distress prior to delivery, in one 200 mg. of meperidine had been administered, and in another there was third-stage hemorrhage. The five remaining deliveries were uneventful. There was no real problem in any of these newborn infants. They responded to suction and stimulation. However, two babies were evaluated as "sleepy." Here, resuscitation with oxygen was more difficult, but the babies responded within several minutes. One case was of relative cephalopelvic disproportion where the delivery was prolonged and difficult. The other was an uneventful labor and delivery. We had one anencephalic newborn infant.

It was noted that in 96% of the patients there was a marked relaxation of the perineum similar to that achieved with spinal anesthesia. The side-effects were few. The most prevalent was a strange congestion of the patient's nose and throat that was described as a tickling, stuffy, choking, or shortness of breath sensation on administration of the drug, lasting less than one minute. Pupillary changes and transient tachycardia[4a] on administration of the drug were noted with some patients.

Comment

Promazine and meperidine in labor afford a method of analgesia and relaxation which appears superior and safer than other modalities in common usage. Ease of administration and minimal side-effects are of particular merit.

The hypotensive effects of promazine and spinal anesthesia do not seem to be significant deterrents to their use. We encountered no clinical hypotension at any time with our methods.

Promazine, in the dosage used, does not appear to result in any marked depressive reaction on the infant at any time, regardless of when administered. The effective duration of action of 50 mg. of promazine given intravenously is about eight hours. In multiparas, the promazine should be administered at the onset of labor. For primiparas, the promazine might well be delayed until the patient shows some discomfort; otherwise, for effective results, the promazine may have to be repeated in eight hours.

The only patients who should be excluded from the promazine routine are those with a history of asthma. We feel that the nasal and throat congestion may be a reflection of the same processes occurring in the respiratory tree of asthmatics. This topic needs further study.

Promazine had a marked relaxing effect on the perineum and a depressive reaction on the vomiting mechanism. It seems also to have some amnesic properties. The reduction of the dosage of meperidine, the elimination of barbiturates and scopolamine, and the minimal use of medications outlined seem to maintain a pleasant and relaxed air in the entire labor suite.

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CARDIAC DISEASE AND HYPOTHYROIDISM

COMPLICATIONS INDUCED BY INITIAL THYROID THERAPY

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Hypothyroidism was treated with desiccated thyroid substance or a rapid acting preparation in nine patients aged 39 to 84 years. The results are presented in tabular form. The treatment was generally effective, but four patients developed cardiac complications which are described in greater detail. Two patients died. In one patient, a woman 69 years old, it appeared that dosages of thyroid substance sufficient to remedy the myxedema could not be given without danger to the enfeebled heart. Intolerance to thyroid medication was most marked in older patients with a history and physical findings of arteriosclerotic heart disease. By commencing with small doses, two patients were enabled to take larger doses which had previously caused angina pectoris and congestive heart failure. Treatment of hypothyroidism in patients of this type should begin with doses of as little as 7.5 mg. of desiccated thyroid daily, with increments of 7.5 mg. every two or three weeks until a dose of 30 mg. a day is reached.

Specific replacement therapy in hypothyroidism quite regularly reverses the disease process in gratifying fashion. Rarely, its use may be attended by development of congestive heart failure, angina pectoris, myocardial infarction, or dissecting aneurysm of the aorta.[1] In our experience during the past three years, four of nine hypothyroid patients developed cardiac complications early in the course of their treatment. This high incidence of adverse reaction stimulated us to review these cases for diagnostic factors in predicting the outcome of treatment. Previous studies [1b] have indicated that a history of hypertension, electrocardiographic abnormalities, or obvious evidence of arteriosclerosis is of little help in predicting complications.

In the review of these cases particular attention was directed to duration of symptoms, severity of hypothyroidism on the basis of clinical and laboratory studies, thyroid preparation and initial dosage schedule, and previous evidence of cardiac abnormalities. Case reports of the four patients in whom complications developed follow.

Report of Cases

Case 1.—A 72-year-old woman had complained of tinnitus, loss of hearing, and cold skin. She denied cardiac symptoms. On physical examination, her skin was dry and her movements sluggish. The thyroid gland was not enlarged on palpation. Her heart was within normal limits.

The protein-bound iodine level was 2 mcg. %, the 24-hour radioactive iodine uptake 16%, the basal metabolic rate (BMR) −29%, and the total cholesterol level 348 mg. %. An electrocardiogram (EKG) revealed ST-T wave abnormalities

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suggestive of myocardial disease. Chest x-ray revealed calcification in the aortic arch and changes consistent with left ventricular enlargement (see figure). Cholecystography revealed cholelithiasis.

Treatment for hypothyroidism was begun with 15 mg. of desiccated thyroid a day and stopped after three days when the patient had chest pain and ST depression (ischemia) on EKG. Treatment was resumed with 7.5 mg. a day, but because of recurrent angina pectoris it was difficult to raise the dose. With very gradual increments of thyroid, a dosage of 45 mg. a day was achieved. At this level of replacement therapy the patient experienced pulmonary edema, which proved responsive to therapy.

She was eventually discharged to the Home Care Program on a regimen of 45 mg. a day, with minimal clinical improvement and no significant change in laboratory values. She was readmitted one year later for gallbladder surgery in the hope that removal of her gallstones might alleviate the angina. During the operation, however, she went into shock and died several hours later. Permission for postmortem examination was not granted.

Significant Clinical and Laboratory

Case	Age, Yr.	Sex	Duration of Disease	BMR, %	Laboratory Values: 24-Hr. Radioactive Iodine Uptake	Laboratory Values: Protein-Bound Iodine Level, Mcg.	Cholesterol Level, Mg. %	History	Cardiac: Blood Pressure, Mm. Hg	Cardiac: Physical
1	72	F	Unknown	−29	16.0	2.0	318	Negative	115/80	Negative
2	63	F	4 mo.	−18	8.5	2.2	234	Negative	130/80	Negative
3	84	F	Several months	−36	9.0	1.5	730	? myocardial infarct; digitalis therapy	120/70	Irregular rhythm, enlarged heart, apical systolic murmur
4	69	F	1 yr.	−25	1.3*	0.6	318	Angina pectoris; digitalis therapy	130/80	Apical systolic murmur
5	64	F	5 yr.	−30	6.0	...	331	Hypertension	200/100	Basal systolic murmur
6	66	F	10-12 yr.	−7	5.0	...	298	Dyspnea on exertion, ankle edema	120/80	Negative
7	39	M	Unknown	−20	20.0†	3.4	200	Negative	120/80	Apical systolic murmur
8	42	M	6 mo.	−13	6.0	2.0	302	Acute rheumatic fever, at age 11	90/60	Enlarged heart
9‡	69	F	6 mo.	−6	...	...	332	Dyspnea on exertion, ankle edema	125/80	Negative

* NSR=normal sinus rhythm; VPC=premature ventricular contractions.
† 48-hour radioactive iodine uptake.
‡ Clinically myxedematous, uncooperative, pretreatment studies incomplete.

Case 2.—A 63-year-old woman was admitted to the hospital because of a urinary tract infection. She complained of constipation for many years and hoarse voice for four months. She denied cardiac symptoms. Her skin was dry and had a yellow tint. Her hair was coarse. The thyroid gland was not enlarged, and cardiac findings were normal on physical examination.

The protein-bound iodine level was 2.2 mcg. %, the 24-hour radioactive iodine uptake 8.5%, the BMR −18%, and the cholesterol value 234 mg.%. An electrocardiogram was within normal limits. Chest x-ray revealed calcification in the aortic arch and a slight increase in the transverse diameter of the heart.

Treatment with desiccated thyroid was begun at a dose of 15 mg. a day, increased to 30 mg. after four days, and to 60 mg. after another four days. Two weeks from the start of the treatment, the patient was noted to have shortness of breath and peripheral edema. Venous pressure was 145 mm. of sodium chloride solution, and the circulation time (arm to tongue) was 22 seconds.

With reduction in thyroid dosage, salt restriction, digitalis therapy, and administration of mercurial diuretics, the patient's signs and symptoms of congestive heart failure disappeared. Subsequently, the dosage of thyroid was more gradually raised without untoward effect. She was discharged to the Home Care Program on a regimen of 90 mg. of thyroid a day and showed moderate improvement.

Case 3.—An 82-year-old woman had had a thyroidectomy performed for thyroiditis nine years prior to admission. Treatment with 60 mg. of desiccated thyroid daily was begun in the postoperative period and was continued until two years prior to admission. At that time, although the EKG failed to show conclusive changes, she was thought to have a myocardial infarction on clinical grounds. Atrial fibrillation was present. Because of mild symptoms of congestive heart failure, digitalis therapy was begun and mercurial diuretics were used in the ensuing two years.

For several months prior to her final admission, the patient complained of progressive weakness, chilliness, dry hair, hoarseness, and constipation. On physical examination the thyroid gland was not palpable. The heart was enlarged to the left anterior axillary line and the rhythm was irregular. There was a harsh systolic murmur at the apex. A trace of pretibial edema was present bilaterally.

The protein-bound iodine level was 1.5 mcg.%, the 24-hour radioactive iodine uptake 9%, the BMR −36%, and the total cholesterol level 730 mg.%. An electrocardiogram confirmed the presence of atrial fibrillation. There were ST-T wave abnormalities suggestive of myocardial disease. A chest x-ray revealed cardiac enlargement in all chambers and calcification in the aortic arch.

Treatment with 5 mcg. of triiodothyronine a day was begun. Four days later the dose was raised to 10 mcg. and after several more days it was increased to 15 mcg. Over this period, the patient's signs and symptoms of congestive heart failure increased markedly and became refractory to treatment. In spite of reduction in dosage of triiodothyronine and rigorous cardiac therapy, she died in congestive heart failure. Permission for postmortem examination was not obtained.

CASE 4 —A 69-year-old woman had a history of hoarseness, partial baldness, coarse hair, anorexia, and intolerance to cold weather for one year In addition, she had noted intermittent ankle edema and symptoms of angina pectoris during this time Physical examination revealed far-advanced myxedema. The thyroid gland was not enlarged to palpation, hearing was decreased on gross testing, and ankle reflexes could not be elicited. Cardiac abnormalities were not noted The protein-bound iodine level was 0.6 mcg %, the 18-hour radioactive iodine uptake 1 3%, the BMR −25%, and the cholesterol value 348 mg.%. The EKG showed T-wave abnormalities suggestive of myocardial disease. Chest x-ray revealed calcification in the aortic arch

Treatment with 15 mg. of desiccated thyroid a day was begun. One week later the patient had an anterior myocardial infarction and thyroid medication was discontinued The patient then refused to eat and became increasingly lethargic and apathetic. This was attributed to progression of the myxedema She died one month after admission

Postmortem examination confirmed the presence of a recent anterior myocardial infarction, secondary to a thrombosis of the anterior descending branch of the left coronary artery In addition, generalized arteriosclerosis and atherosclerosis of the aorta with medial calcification were noted The thyroid gland was atrophic and fibrotic

Data in Nine Patients with Hypothyroidism

EKG*	Radiology	Treatment	Result
NSR, ST T wave abnormalities	Left ventricular hypertrophy, calcification in aortic arch	See case report	Angina, died after operation
NSR, normal	Increase in transverse diameter of heart; calcification in aortic arch	See case report	Congestive heart failure, living
Atrial fibrillation; ST-T wave abnormalities, low voltage limb leads	Enlargement of all cardiac chambers, calcification in aortic arch	See case report	Congestive heart failure, died
NSR, T wave abnormalities	Left ventricular hypertrophy, calcification in aortic arch	See case report	Myocardial infarct, died
NSR, ST-T wave abnormalities, suggestive of left ventricular hypertrophy	Left ventricular hypertrophy, dilated ascending aorta	30-60 mg of desiccated thyroid stopped and resumed on several occasions	No complications, living
NSR, T wave abnormalities	Left ventricular hypertrophy	90 mg of desiccated thyroid for 10-12 yr.	No complications, living
Sinus tachycardia, normal	Normal	15 mg of desiccated thyroid/day, raised after several weeks: 60 mg at present	No complications, living
Sinus bradycardia 1st degree heart block, intraventricular heart block, low voltage limb leads	Left and right ventricular hypertrophy	7 5 mg of desiccated thyroid/day for 7 days; 15 mg for 7 days; 30 mg for 20 days; then 60 mg ; present dose 120 mg /day	No complications, living
Sinus tachycardia with rare VPC, ST T wave abnormalities	Increase in transverse cardiac diameter	Triiodothyronine, 12 5 mcg /day; 4 days later ? thyroid storm, then desiccated thyroid, 7 5 mg for 3 weeks, 7 5 and 15 mg on alternate days for 2 weeks, then 15 mg /day	Psychotic, in state hospital

The microscopic description of the aorta and myocardium is of interest. The wall of the aorta was thickened with atheromatous plaques consisting of foam cells and cholesterol crystal clefts The media revealed interstitial collections of basophilic mucoid material and small ovoid cyst-like spaces containing similar material. The myocardial fibers appeared enlarged and in several areas the myofibrils had disappeared, leaving a collapsed collagenous stroma. In some places there was an increase in interstitial connective tissue

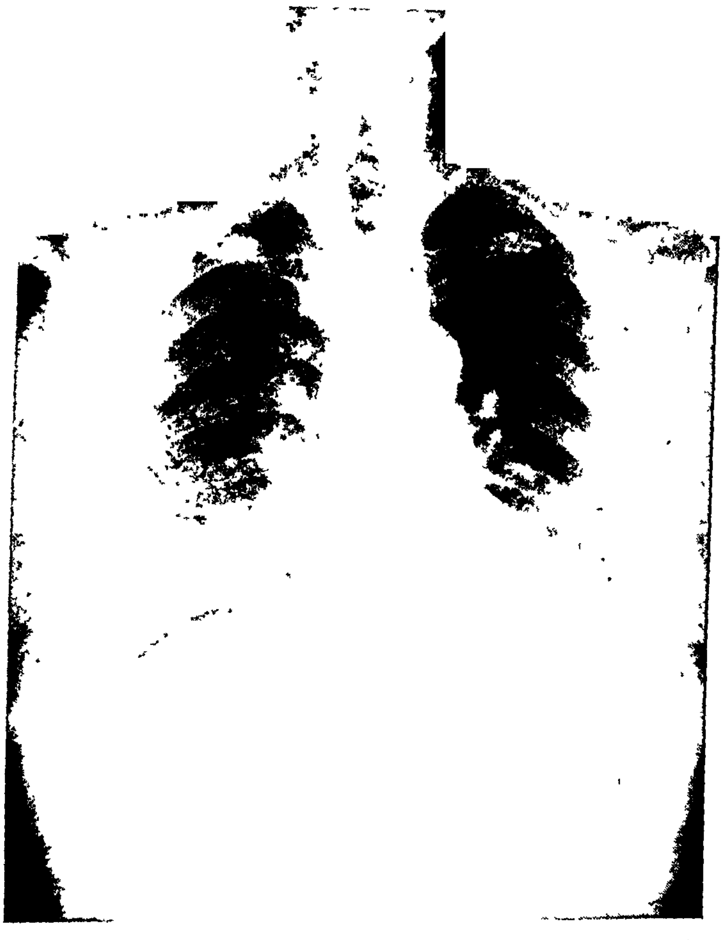
Comment

It should be noted that the cardiac complications seemed related to initial vigorous treatment rather than total dosage. In the two patients who survived such complication, reduction in dosage and then more gradual increments were well tolerated. The final dose was larger than that at which cardiac symptoms were first manifest. There was no striking difference in cholesterol values between those patients who developed cardiac complications and those who did not. The hypothyroidism was similar in duration and severity in all patients except the patient in case 4 who had far-advanced myxedema. The predominance of females in both groups reflects the sex incidence of hypothyroidism. The table summarizes the significant features in all nine patients.

In three respects the groups differed. Those who developed cardiac complications were, in general, older than the other group, with a mean age of 72 as compared with 56 years. The cardiac history in two of these patients indicated the presence of arteriosclerotic heart disease. In addition, calcification in the aortic arch was only present radiographically in the patients who later went on to develop complications. The latter finding is nonspecific and may be expected in a significant percentage of any group of patients over the age of 50. It implies arteriosclerosis elsewhere and suggests its presence in the coronary arteries. This correlation was confirmed by postmortem studies in case 4 in which generalized arteriosclerosis, coronary arteriosclerosis, and medial calcification of the aortic arch were noted.

There has been much interest in the relationship between hypothyroidism and arteriosclerosis.[2] The hypercholesteremia of thyroid insufficiency may be important in this regard. The role of concomitant hypertension in the production of arteriosclerosis in hypothyroid patients has also been implicated.[3]

The hypothyroid patient often presents a precarious cardiac problem in other respects. Classic clinical myxedema, in which there are right-sided and left-sided dilatation, feeble cardiac pulsations, usually associated with abnormalities of conduction and low voltage on the EKG, and definite reduction in cardiac size after administration of thyroid extract, is relatively uncommon. However, the heart in hypothyroidism is frequently enlarged and heart failure may be imminent or present.[4] Grossly, there may be cardiomegaly and atheromatous changes in the coronary arteries. Pericardial effusion may be present more often than suspected.[5] Histologically, the muscle fibers may be swollen and vacuolated with loss of striation.[6]



Chest x-ray (case 1) showing calcification in aortic arch. Cardiac contour suggests ventricular hypertrophy.

In patients with hypothyroidism an increase in heart size of this nature is often tolerated, partially because of concomitant reduction in total body metabolism. The circulation of hypothyroid patients may undergo profound change. The heart rate and cardiac output decrease; the velocity of the blood flow is retarded; and arteriovenous oxygen difference increases.[7] The converse is true in patients with thyrotoxicosis or with hypothyroidism under treatment. Increased tissue respiration of cardiac muscle has been demonstrated in thyrotoxic animals[8] and humans.[9] With thyroid therapy, reduction in heart size is a gradual process, during which signs and symptoms of angina pectoris or myocardial failure may be precipitated.[10] Initial overtreatment with thyroid preparations in hypothyroid patients with possible heart disease may cause an enlarged heart to function above its physiological capacity. It may be postulated, therefore, that metabolic demands precede cardiac improvement. On the other hand, cautious treatment may often relieve the symptoms of congestive heart failure[4] or coronary artery disease.[11] Increased cardiac function is a prerequisite to the increase in tissue demands for the achievement of a stable thyroid-cardiac relationship.

In 1925, Christian[12] stressed the necessity for small initial doses and gradual increments in thyroid therapy, particularly in the older age group. With the recent introduction of rapidly acting thyroid preparations, this note of caution needs reemphasis. Particular application may be found in those patients with signs of arteriosclerosis.

In patients with possible heart disease it seems reasonable to begin treatment with a dose as low as 7.5 mg. of desiccated thyroid daily, with increments of 7.5 mg. every two to three weeks until a dose of 30 mg. a day is reached. Then larger increments may be used until the achievement of a euthyroid state. The slightest indication of cardiac difficulty should prompt a reduction in dosage schedule.

Summary

Specific replacement therapy in hypothyroidism often gives rise to cardiac complications. Four case reports of patients in whom such complications developed during thyroid treatment were compared to a group of five patients in whom treatment caused no difficulty. The complications seemed related to initial vigorous treatment rather than total thyroid dosage. Arteriosclerotic heart disease increases the risk of such treatment. Its presence, particularly in an older age group, may be implied by evidence of arteriosclerosis in other sites.

In hypothyroidism, anatomic changes in the heart may occur. They may be tolerated due to concomitant circulatory changes and reduction in total body demands. Thyroid therapy reverses these changes and may cause an enlarged heart to function above its physiological capacity. For these reasons, therapy in patients with possible heart disease should be instituted with low doses and gradual increments.

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This study was supported in part by grants from the New York Heart Association and the U. S. Public Health Service.

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CLINICAL NOTES

NERVE DEAFNESS ASSOCIATED WITH CONGENITAL SYPHILIS

REPORT OF A CASE TREATED WITH PREDNISONE AND PENICILLIN

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The nerve deafness of late congenital syphilis is usually an isolated neurological finding without concomitant evidence of neurosyphilis and without abnormalities in the cerebrospinal fluid. Keidel and Kemp[1] found 22 such cases among 230 patients with congenital syphilis. In contrast to most of the manifestations of syphilis, which respond to treponemicidal therapy and which can be attributed to the direct destructive effects of Treponema pallidum, the nerve deafness of late congenital syphilis does not respond to such therapy.[2] The scantiness of the postmortem material available permits no certain conclusions about the pathology or even the anatomic site of the lesion.

Interstitial keratitis and Clutton's joints (intermittent hydrarthrosis of the knees), both manifestations of late congenital syphilis, behave like hypersensitivity phenomena in that they are resistant to therapy with penicillin but responsive to that with corticosteroids. In speculating about the nature of late isolated nerve deafness in congenital syphilis, we have wondered whether it might behave in similar fashion. It was this possibility which induced us to treat with prednisone the patient here reported. The results were unexpected and, indeed, rather startling.

Report of a Case

A girl, born in 1938, first visited Johns Hopkins Hospital at the age of 9, complaining of a sore throat. Because the result of a routine serologic test for syphilis (STS) was positive (titer at 48 units), she was referred to the syphilis clinic. According to the mother, who had been inadequately treated for syphilis during the pregnancy with this child, the patient had shown no abnormalities in infancy. Findings on physical examination in April, 1947, were normal. The spinal fluid contained 18 cells per cubic millimeter and 53 mg. per 100 cc. of protein; the Wassermann reaction was positive down to 0.1 ml. Accordingly, she was treated with 1,522,500 units of penicillin in 125 doses every two hours by intramuscular injection and eight malarial paroxysms. Six months later, she returned with active interstitial keratitis in the left eye. At this time a further 60 million units of penicillin was administered over a period of seven and one-half days. The keratitis gradually cleared. She complained of some deafness at about this time. An otologist could find no abnormalities, but audiometry was not performed. One year later (November, 1948) she developed mild interstitial keratitis in the right eye, but this cleared without further antisyphilitic treatment.

In April, 1950, she again complained of poor hearing, this time confirmed by an otologist, who found mild "mixed deafness," more marked in the right ear. The following

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September, she underwent adenoidectomy, but, despite this, in March, 1951, she had a temporary deterioration of hearing and was equipped with a hearing aid, which she learned to use successfully. Results of audiometric testing at this time are shown in figure 1. In the next five years, she was under periodic observation in the otolaryngology clinic.

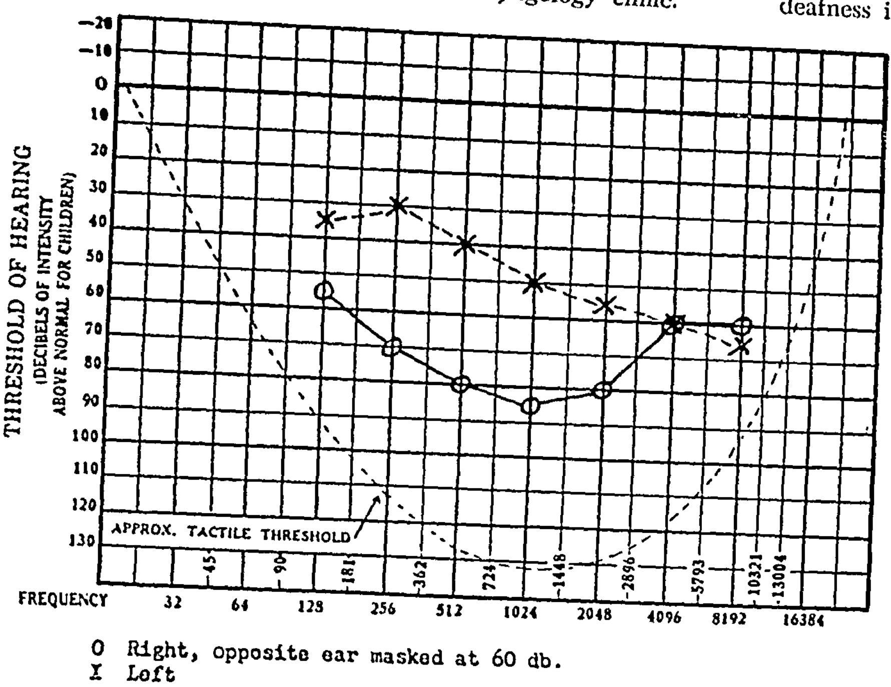


Fig. 1.—Results of audiometric testing six years prior to sudden deterioration in hearing. Speech reception threshold: 94 db. on right, 54 db. on left; discrimination score: could not do on right, 74% on left.

In 1953, she was given 1,800,000 units of penicillin for a sore throat and 1,200,000 units for pelvic inflammatory disease acquired shortly after the first of her many sexual exposures. At about this time, she was, for a short period, under psychiatric care for a transient behaviour disturbance.

On Sept. 7, 1956, she was seen in the syphilis clinic. On the previous day she had awakened with complete inability to hear and marked tinnitus. She had had no antecedent illness and there were no heralding symptoms. She had no dysphasia, nausea, vertigo, headache, or defect of balance. Detailed examination of the nervous system then and on four later occasions revealed no abnormalities other than those related to nerve deafness. Labyrinthine function was not tested. The spinal fluid was completely normal, and the titer of reagin in the blood, which, since 1953, had been 4 units or less, showed no rise then or subsequently. Audiometry (fig. 2) revealed that she could hear loud sounds, and there was very little deterioration in her hearing acuity for pure tones, whether this was assessed by conscious cooperation or by psychogalvanometric skin resistance tests. The speech awareness threshold, a measure of her ability to recognize that someone was speaking (indicated by the dotted line in figure 3), was almost unchanged, but no amount of loudness enabled her to identify individual words. In short, verbal communication with her was completely impossible. For this reason neither the speech-hearing threshold (the level of loudness at which one can identify 50% of spondaic words) nor the discrimination score (the percentage of one of a number of standard lists of 50 words which one can identify at a level of 30 db. above the speech awareness threshold) could be measured. Because hearing in the right ear had previously been very poor, it is not certain whether this acute deterioration involved both ears or only the left. The audiometric findings indicated that this episode was not, like her antecedent deafness, a simple abnormality in the end-organ but, rather, a complex neural deafness involving principally the interpretation of sound.[3]

It seemed impossible that this deafness could have been due directly to treponemal activity. Her congenital syphilis had been treated with nearly 65 million units of penicillin, and reinfection, a rarity in congenital syphilis,[4] could be excluded by lack of clinical evidence of early syphilis, failure of the STS titer in the blood to rise, and the presence of a normal spinal fluid.

Thirty-six hours after the onset of symptoms, therapy with prednisone was started. She received 30 mg. per day for two days and thereafter 20 mg. daily. As a precaution, 6 million units of penicillin was given in seven doses.

The results of treatment are outlined in diagrammatic form in figure 3. Improvement was prompt; verbal communication was possible by the 7th day, and by the 14th day she could understand most of what was said to her in a loud voice. On the 18th day she could tolerate audiometry, and thereafter there was continued improvement. From the 39th day onward, the dose of prednisone was gradually reduced until she was taking 5 mg. daily (95th day). At this point there was marked subjective deafness (audiometry showed it to be comparatively slight), and the previous heavy doses were resumed. In late December, 1956, without seeking advice she cut down her dose to 2.5 mg. daily. There were no ill-effects, but because of the risk of acute adrenal insufficiency full doses were once again employed. After this, progress was uneventful and the dose of prednisone was tapered cautiously until June 1, 1957, when it was stopped. An illustrative test result is shown in figure 4. She was seen several times subsequently, most recently in April,

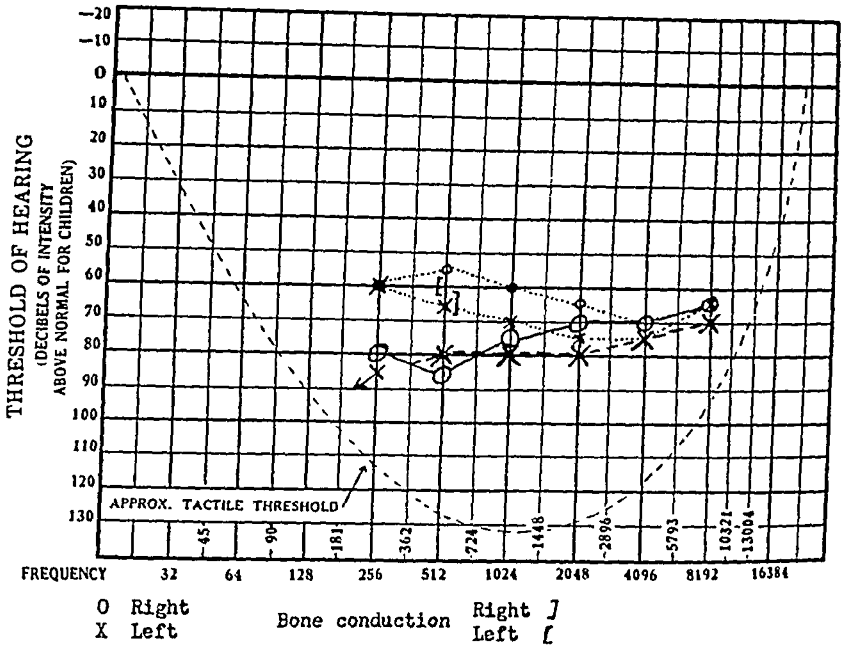


Fig. 2.—Results of audiometric testing four days after sudden deterioration in hearing. Dotted lines refer to hearing by bone conduction. There is little change in pure tone hearing. Neither speech reception threshold nor discrimination score could be obtained, except for awareness at 54 db. on left in speech reception.

1958, when audiometry revealed that her hearing was as good as it had been before the sudden deterioration on Sept. 6, 1956.

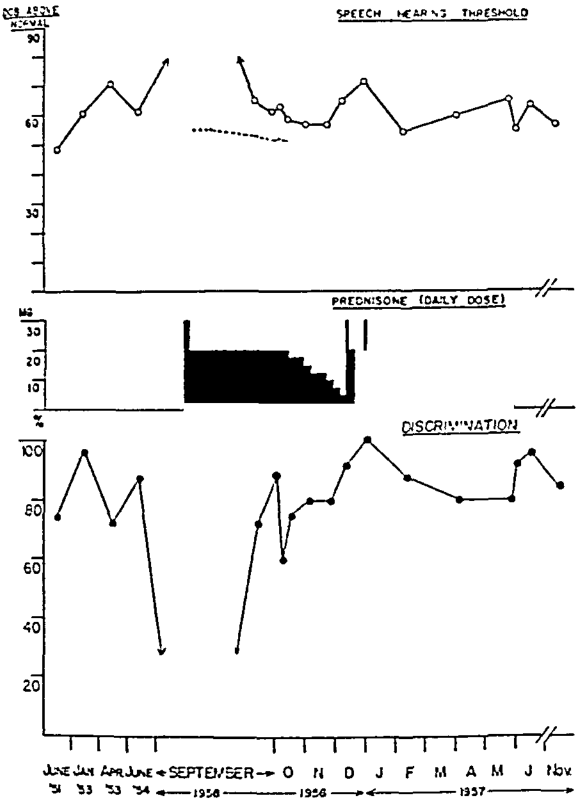
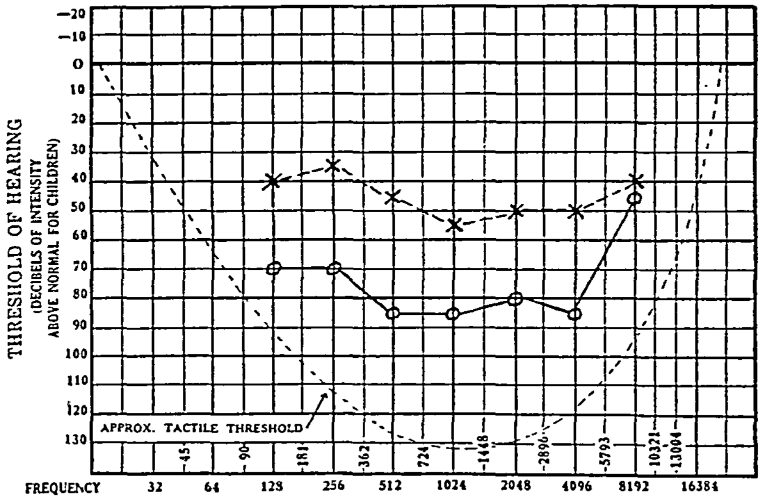


Fig. 3.—Interpretation of speech. Dotted line represents speech awareness threshold. At height of deafness it was not possible to perform tests of interpretative function. Progressive increase in loudness of testing sound produced pain before any words could be distinguished.

Comment

The validity of this case report is contingent on three facts: proof of congenital syphilis, proof of the etiology of the deafness, and proof of the therapeutic effect of prednisone. Of the first of these there can be no doubt. Her mother was known to have had inadequately treated syphilis during the pregnancy with this child, and the patient herself was observed to have interstitial keratitis and, at an early age, a positive STS result in her blood and spinal fluid. Of the second, there can be little doubt. Sudden severe exacerbation of nerve deafness when she was 18 years old, in the absence of other signs, spinal fluid changes, history of trauma or drug ingestion, or antecedent viral or bacterial infection, permits of no other ready explanation on an organic basis. Conversion hysteria can almost certainly be ruled out by the pattern of the audiometric findings and the rapid response to treatment without any form of psychotherapy. Moreover, Hallberg [5] found a psychological cause in only one of 178 consecutive cases of sudden deafness from all causes. It seems probable that there was no serious bias in the source of his material. Proof of the effectiveness of the prednisone is also reasonably certain. In our experience, in the extensive files of the syphilis clinic of the Johns Hopkins Hospital, and in the world literature, we have encountered no case with spontaneous improvement comparable to this, though it is clear that some fluctuation in the degree of deafness may occur from time to time in many cases. It seems most unlikely that penicillin was the responsible therapeutic agent. She had already received nearly 65 million units of penicillin before this severe exacerbation, and comparably dramatic effects from treponemicidal therapy of severe deafness in late congenital syphilis do not appear to have been observed previously. Moreover, long after the penicillin therapy had been stopped tapering of the dose of prednisone appears to have resulted in a mild relapse, which responded promptly to resumption of full dosage. Perlman and Leek [6] treated five of their series of patients with established nerve deafness in late congenital syphilis with ACTH and penicillin, with some improvement in three. None of their patients was seen after sudden loss of hearing. These writers thought that the ACTH, by reducing inflammation and fibrosis, enabled the penicillin more easily to reach treponemes, which they believed were still present.

Since the incidence and prevalence of congenital syphilis is decreasing, it is unlikely that any one



O Right, opposite ear masked at 70 db.
X Left

Fig. 4.—Results of audiometric testing 14 months after episode and 5 months after prednisone therapy had been stopped. Function had been restored to its previous level. Speech reception threshold: awareness at 74 db. on right, 54 db. on left; discrimination score: could not do on right, 84% on left.

observer will compile a large series of cases with sudden nerve deafness, due to this disease, in the acute phase. Steroid therapy has proved so effective in this case that we recommend that others who encounter such cases try its effect.

We have had no experience with the use of prednisone in chronic syphilitic nerve deafness or in chronic deafness from other causes, and we are in no position to express an opinion as to whether it would be of value. There is on record at the Johns Hopkins Hospital, however, a well-documented case of sudden partial perceptive deafness in a young woman immediately after a virus infection. It appears that prompt steroid therapy resulted in dramatic improvement in this case, but in sudden nerve deafness of nonsyphilitic origin spontaneous improvement is known to occur.

Summary

A girl with congenital syphilis received, between the ages of 9 and 15 years, several courses of therapy with penicillin, to a total of 65 million units. At the age of 18, without evidence of reinfection, she developed complex nerve deafness sudden in onset. She was treated with prednisone and penicillin with success. There is evidence that the improvement was not due to the penicillin or to coincidence. It is not suggested that steroid therapy would prove effective in long-established syphilitic deafness or chronic nerve deafness from any other cause.

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SPECIAL ARTICLE

COMMON SENSE APPROACH TO THE PROBLEM OF GENETIC HAZARD DUE TO DIAGNOSTIC RADIOLOGY

REPORT BASED IN PART ON STUDY OF EXPOSURES IN A SMALL AMERICAN INDUSTRIAL CITY

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Accumulating evidence suggests that the genetic damage to the human gonads due to exposure to ionizing radiation is greater than previously thought. This, with the greater potential for exposure of whole populations in medicine, industry, and defense, has resulted in increasing concern over genetic injury to whole populations. Debates among scientists over the amount and effect of radiation due to fall-out from testing atomic weapons have made the American public more aware of the hazards of radiation. This is a healthy state of affairs, if perspective can be maintained on the part of both the medical profession and the public.

Considering the relative genetic hazards to whole populations from man-made radiation, we find that by far the largest contribution comes from diagnostic radiology. At the same time, the judicious use of diagnostic radiology is one of medicine's most important tools.

Much remains to be learned regarding the actual exposures being received and the genetic consequences. However, as discussed later, there is increasing evidence that any exposure of the gonads to radiation is harmful and should, and can, be greatly reduced by techniques and methods that are already available. The dangers from radiation have received so much publicity that an appreciable number of individuals have been frightened to the point of refusing very desirable roentgenologic examinations.[1]

This discussion will attempt to present a common sense approach in limiting exposure to the gonads without sacrificing the tremendous value of diagnostic x-rays. Somatic damage to individuals, while of great significance, is given little or no consideration in this discussion simply because this is an-

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Read before the Annual Industrial Health Conference, Atlantic City, N. J., April 23, 1958.

other subject. Suggestions are based on an evaluation of the genetically significant radiation dose from the diagnostic use of x-rays in a small American city,[2] as well as on preliminary national studies which have been made in the United States and abroad.[3]

Several geneticists[4] have sketched the background which has lead to the concern of this study. Briefly, realization that radiation increases the mutation rate dates back 30 years to Muller's experiments with fruit flies.[4c] Spencer and Stern,[5] using more than 50 million flies, showed that genetic damage was proportional to dosage in the important range of 25 to 50 r. Concern has been heightened by recent findings[4f] that exposure of mice to a given quantity of radiation increases the mutation rate by about 15 times as much as does an equal exposure of Drosophila, which had formerly served as the sole basis for inferring human risks.

Quantitative Estimate of Genetic Damage

While there is general agreement that any radiation exposure is harmful from a genetic standpoint, it is not possible to say with any assurance how harmful. According to Crow,[4a] the spontaneous mutation rates in man, which have been measured, average 10 to 15 per million genes. In mice the average rate of x-ray-induced mutation is about one per million genes per 4 r.[4f] If human genes have the same response to x-ray exposure as do those of mice, 40 to 60 r would be required to double the present mutation rate.[4a] Both the National Academy of Science (NAS) and the British Medical Research Council have suggested 30 to 80 r as the range within which the doubling dose is likely to be.[3]

Consequence of Doubling Rate of Mutation.—One may reasonably ask, what is the consequence of doubling the present spontaneous rate of mutation? Two aspects must be considered: the effect on the immediate offspring and the effect on later descendants.

The British study[3b] estimates that only about 1% of mutant genes are dominant and cause damage in the next generation. From calculations based on theory, about 10% of germ cells at present carry a new mutation. Hence, doubling the mutation rate might lead to an increase of one in a thousand (0.1%) in the number of harmfully affected children in the next generation. In Richland, Wash., during the years 1953 to 1956, inclusive, newborn infants with obvious mental or physical defects, as indicated by the obstetric records, amounted to 0.65% of the births. However, the usual estimate is that about 2% of all babies have some observable genetic defect at birth, while a considerable number develop diseases or abnormalities in which hereditary constitution is a preponderant cause.[4a]

The consequence of one generation of parents exposed to 10 r in the United States, if we apply the above assumption, would be that with the present births of about 100 million per generation there would be 400,000 (10/50 by 2% by 100 million) babies with new severe genetic defects. These would be spread over many generations, with perhaps 10% (40,000 severe defects) occurring in the first generation.[4a] This would be an increase of some 1,300 severe defects (1 in 2,500 births) per year. The factor of uncertainty in this figure would be very high.

The British report estimates that the risk that a pair of parents will produce an imbecile or idiot, that is, a child with a severe mental defect, who survives is about 1 in 500. The increased proportional risk for parents in both of whom mutation rates have been doubled is about 3%. This means that the risk of having a child with severe mental defects who survives would be 1 in 485.[3b]

On the basis of experience with fruit flies, we would expect that the most frequent human mutations would not cause gross physical abnormalities but minor impairments of body functions leading to such factors as increased susceptibility to disease, decreased vigor and productivity, and shorter span of life.[4a] The National Academy of Science Genetics Committee[3a] reports that, roughly, one child in 20 would have an additional mutation if the whole population of the United States now received a genetically significant gonad x-ray dose of 10 r. The uncertainty of this estimate was said to be about a factor of 10, and the factor of uncertainty is even greater in trying to evaluate actual impact, in terms of disease and disability, of these mutations on subsequent generations.[4e]

It should be remembered that there are many factors other than radiation which cause genetic changes in laboratory animals, and presumably in man, such as temperature, oxygen tension, and various chemicals. Based on data from fruit flies and the fact that wearing of clothes increases male gonad temperature by 3 C, Ehrenberg and coworkers feel that wearing clothes may cause almost half of the present load of spontaneous mutations. They recommend the wearing of kilts as most important in reducing male gonad temperature and hence in decreasing mutations.

Aging due to Radiation

Studies suggest that mutational changes induced by radiation in the germ line materials of past generations may combine with the mutational changes induced by radiation in the soma of the present generation to influence the time of death.[7] Warren[8] reports a shorter life span for radiologists as compared with other physicians, while Lewis[9] has questioned the statistical validity of Warren's conclusions on the basis that age differences alone in the groups being compared would be sufficient to account for the difference in average length of life. Braestrup[10] points out also that, in years past, radiologists using nonprotective equipment were exposed to radiation of the order of 100 r per year, while with present standards of protection the yearly dose is reduced to about 1 r per year.

Failla and McClement[7a] estimate a possible life shortening of one day per roentgen exposure, while the estimate of Jones[11] is higher. Such figures must be considered in light of some of Jones' other estimates of average loss of life span, such as loss of 18 years due to smoking two packages of cigarettes per day, 15 years due to being 67% overweight, and 15 years due to having highly elevated lipoprotein level.

Blair,[12] from a careful analysis of animal studies, has pointed out that radiation injury has two components: a reparable one and an irreparable one. Failla[7b] postulates that the irreparable component is the result of direct interference with the chemical processes of the cell at one or more links in the chain. Several authors feel that, in the absence of disease, ionization by radiation is one of many processes which may shorten the inherent life span determined by the genetic constitution inherited from the parents.[13] This is said to be due to an acceleration of the aging process as a result of deleterious somatic cell mutations. It is hoped that statistics from Hiroshima and Nagasaki may add to our knowledge in this field. At present, inferences are largely based on animal studies.

New Permissible Limits Emphasize Population Exposures

The genetic harm to a population due to radiation is roughly proportional to the total radiation received by the gonads between conception and reproduction. This is true irrespective of how or at what intensity the radiation is received or how it is distributed among the individuals of the population. Exposure of 100 young people to 1 r each has essentially the same effect on the germ pool as does exposure of one young person to 100 r. Taylor[14] has nicely traced the changes in knowledge and conditions leading to changes in recommendations of the National Committee on Radiation Protection (NCRP)[15] and the International Commission on Radiation Protection (ICRP) during the last 25 years as far as occupational exposure is concerned. At a meeting of the ICRP in April, 1956, the genetic problem was considered, and a figure of about 10 rem of man-made radiation was recommended as a reasonable average per capita dose to the age of 30 for the future for the total population. It has been decided by the NCRP, on the basis of present evidence, that the most important new limitation in industrial exposures should be one relative to gonadal exposure to individuals during the reproductive period. The NCRP report stated, "If we allow an accumulated dose, over fifty years, of about 250 rem up to age 70, this would amount to an average of about 5 rem/year. The new requirement will be that, at a given age of 18 or over, an individual may be allowed to accept a dose such that his total accumulation in rem will not be in excess of 5 times the number of years of age over 18. Thus, at any time, exposure must be less than 5 (N–18) rem where N represents the person's age. This automatically holds down exposure at the younger ages where it is most critical. It gives leeway at the older ages, where it is less critical."

The carefully operated industrial facility should have little difficulty in meeting these recommended limits. Even though enormous quantities of radioactive material were processed at the Hanford Atomic Product Operation during 1957, the average annual whole-body exposure to external radiation of individuals in the monitored areas was 0.30 rem per man-year. It is estimated that this is about the same as the gonad exposure. Annual chest x-rays constitute a part of the health inventory for all employees. In addition, regional roentgenograms are taken as needed in work placement or in handling occupational injuries. Such diagnostic procedures for employees resulted in an average annual gonad exposure of 0.03 rem per employee (1953-1956, inclusive), in addition to that which was received in the plant. Total employee annual exposure was 0.30 rem within the plant plus 0.03 rem from employee diagnostic procedures concerned with employee health maintenance. As a result of this study, a small bag lined with rubber lead sheet equivalent to about 1 mm. of lead is now being used to protect male gonads during diagnostic work involving the low part of the back, hip, pelvis, and low part of the abdomen, and this is expected to eliminate a great deal of the gonad exposure, since most of the procedures involving these areas are in male employees.

Lincoln and Gupton[16] estimated employees annual gonad exposures from diagnostic x-ray procedures both inside and outside the plant as 0.016 r at the Oak Ridge National Laboratories.

If such conditions are maintained as atomic industry expands, the contribution of gonad exposure in industry spread over the general population would be very small compared to that of diagnostic exposure. Even assuming there were a million radiation workers (0.6% of the present population of 160 million), this would only amount to 0.06 rem (0.33 r by 30 by 0.006) for a 30-year period, if exposures in other installations are similar to those at Hanford.

Critical Evaluation of Diagnostic X-ray Procedures

A number of studies are in progress to try to determine the genetically significant radiation dose which is being received by the people of various countries through the diagnostic use of x-rays.[17]

This is compared with the natural contribution as well as other sources of man-made radiation. The report of the British Medical Research Council,[3b] covering England and Wales, and the preliminary report of the American National Academy of Sciences, National Research Council,[3a] are notable examples of such studies.

United States Study.—The preliminary report by Laughlin and Pullman [18] for the National Academy of Science states that the genetically significant dose will be that which is delivered to the gonads of the patients under 30 years of age. This carries the average parent up to the mid-productive period and so represents approximately the average annual genetic dose. A more accurate method for taking into account the genetic effects is to weight the gonad dose each person receives up to a given age by the probable number of children to be born subsequently to the person. This procedure was used first in the Australian study [17h] and later in the British study [17i] and is used in the study in Richland, Wash.[2] The NAS [18] estimate of the average gonad dose which Americans receive from diagnostic procedures during the first 30 years of life is 4.1 r and for x-ray and radioisotope therapy, 0.5 r. It is further estimated that the exposure would be reduced to 1.5 r for diagnostic exposures if computations were based on the lowest gonadal doses reported. The NAS estimate, therefore, is that gonad exposure from diagnostic radiation is a little greater than that from natural radiation (3.1 rem).

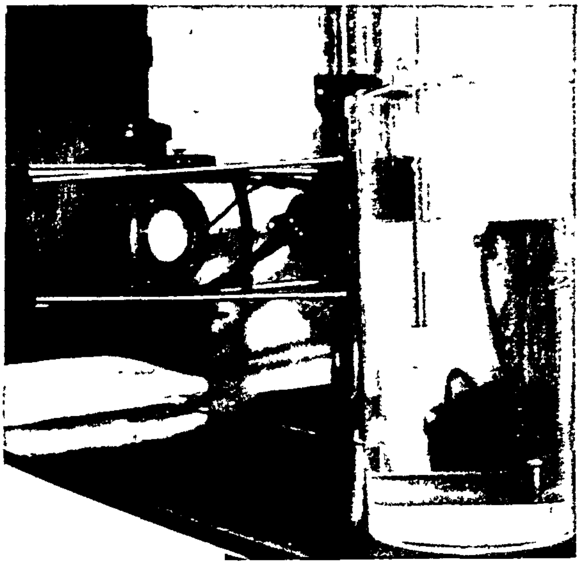

Fig. 1.—Water-filled Lucite container used as phantom to simulate tissue of female torso. Adjustable meter is located at approximate position of gonads and registers dose during various roentgenologic procedures.

Richland, Wash., Study.—Richland, Wash., is the resident community for the employees of the Hanford Atomic Products Operation, where plutonium is manufactured by the General Electric Company for the Atomic Energy Commission. All x-ray diagnostic procedures performed in Richland (population 26,740) for a four-year period, 1953-1956, inclusive, have been tabulated. These are subdivided according to sex, part of body examined, and age group (fetus, 0-1, 2-9, 10-15, 16-20, 21-25, 26-30, 31-35, 36-40, 41-45, and 46 years and over). About 85,000 examinations were tabulated. Most of the x-rays were taken in the 109-bed, privately operated Kadlec Methodist Hospital, under the direction of a specialist in radiology. About 10% of the total exposure came from the offices of a private radiologist, a general physician, a chiropodist, and a facility for dental x-rays and from one chest survey by a mobile unit. In diagnostic procedures, where exposure to the direct rays is high, measurements were made to determine the gonad dose. Measurements were also made of gonad dose and lung dose during chest x-rays, because of the frequent use of this examination. Measurements were made on the hospital machines, since 90% of gonad exposures originated here. Measurements on the private radiologist's machine showed exposures about 40% lower than those of the hospital machine. The hospital measurements were used in calculating all of the exposures, as the private radiologist's machine was tested after the results had been summarized and the degree of accuracy of results does not warrant corrections which would modify the final result by only about 2%.

For the measurement of the dose to the female gonads, a water-filled Lucite (polymerized methyl methacrylate) phantom, 12 in. in diameter and 24 in. high, was used (fig. 1). This simulates human tissue with reasonable accuracy. A 5-r Victoreen roentgen meter chamber was covered by a rubber balloon and immersed in the water at measured positions. It was assumed that the ovaries are located 12 cm. from the anterior surface and 8 cm. from the posterior surface. The ovaries are usually 4 to 5 cm. from the mid-line, but instead of measuring the dose for right and left side an average depth of 12 cm. for lateral exposures was assumed. The water phantom was placed in the patient's position, and simulated x-ray exposures were made of the anatomic part to be examined.

For the male gonad measurements, a Masonite phantom with rudimentary legs was used (fig. 2). The spermatic tissue is distributed throughout the testis to a maximum depth of 12 to 20 mm. and to a minimum of 1 to 2 mm. It was assumed that for direct anteroposterior exposures the average depth was 7 mm., which makes a small allowance for shielding by nearby tissues. The dosimeter was covered by ¼-in. of Lucite to simulate this depth of tissue.

Table 1 gives the gonad dose for several common examinations for males and females, annually for an average year, obtained by dividing the four-year exposure by four. It may be seen from this table that the examinations of the low part of the back and abdomen and of the pelvis and hips constituted only 6% of the total number of examinations but contributed 77% of the total dose to the gonads. This is because the gonads are exposed to the direct x-ray beam during these examinations.

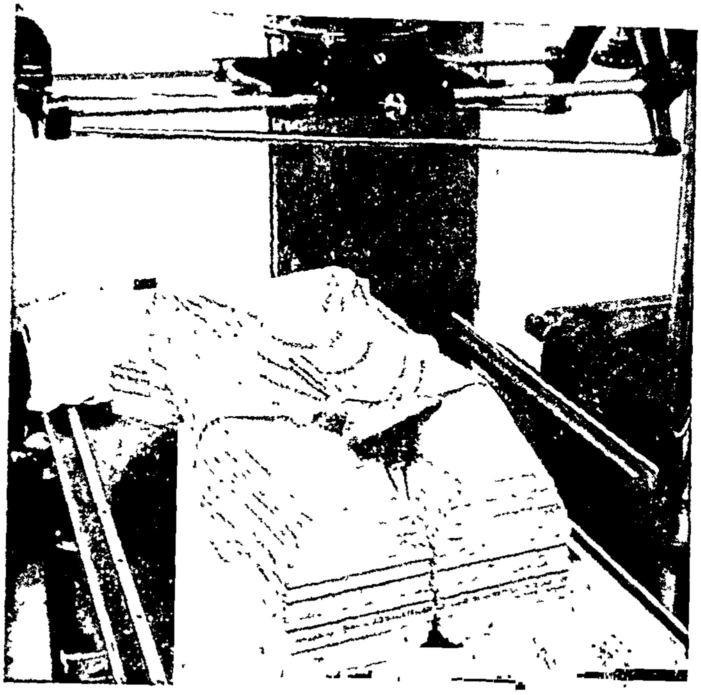

Fig. 2.—Laminated Masonite form used to simulate male torso in determining gonad doses. Lead-lined pouch for protection of male gonads during diagnostic procedures is shown with meter in place to measure degree of protection afforded.

Table 1.—*Measured Gonad Exposures During Some Common Roentgenographic Examinations at Richland, Wash., 1953-1956 (One-Year Average from Four-Year Period)*

	Gonad Exposure Per Examination, Mr*			Total Annual Exposures, Mr	% of All Examinations	% Contribution to Total Exposure
	Male	Female	Fetus			
Chest photofluorogram, 4 × 5	6.7	3.0	3.0	21,003.0	20.5	1.07
Chest roentgenogram, 14 × 17	0.6	3.3	3.3	14,932.0	26.8	0.76
Skull or sinus†	1.0	0.25	0.25	315.0	2.2	0.02
Finger, wrist, or elbow†	0.3	0.06	0.06	207.0	4.2	0.01
Knee or femur†	2.5	1.25	1.25	894.0	2.0	0.05
Dental, full†	15.0	2.5	...	7,592.0	13.8	0.39
Lumbar spine	128.0	1,320.0	1,320.0	143,226.0	1.3	7.28
Lumbosacral spine	82.0	2,800.0	2,800.0	136,238.0	0.08	6.93
Sacroiliac spine	3,000.0	1,950.0	1,950.0	75,863.0	0.13	3.86
Pelvis	2,600.0	1,300.0	1,300.0	152,450.0	6% 0.39	77% 7.75
Pelvimetry	...	2,160.0	2,160.0	61,020.0	0.13	3.10
Hips	3,250.0	1,625.0	1,625.0	221,031.0	0.46	11.24
Barium enema, GI fluoroscopy	360.0	1,680.0	1,680.0	732,200.0	3.4	37.23
Mass miniature radiography†	1.5	1.5	...	3,198.0	9.98	0.16

* Individual measurements for adults.
† Taken from literature—others measured.

The genetically significant radiation has been calculated by factoring in the risk of subsequent parenthood for the diagnostic exposures and for exposures from natural radiation. These calculations and the technical details of the study are reported in another paper.[2] The genetically significant exposure from diagnostic radiation is then compared with the genetically significant natural radiation for Richland, Wash.

$$\frac{\text{Annual genetically significant diagnostic radiation per person}}{\text{Annual genetically significant natural radiation per person}}=\frac{91\text{ mr}}{204\text{ mr}}=0.45$$

If we assume that the genetically significant radiation is that received annually by the population of Richland during the first 30 years of life, we have this result:

$$\frac{\text{Diagnostic radiation per person per year (first 30 years of life)}}{\text{Natural radiation per person per year (first 30 years of life)}}=\frac{46\text{ mr}}{104\text{ mr}}=0.44$$

When these two results are compared, the ratio of diagnostic radiation exposure to natural radiation exposure differs by a factor of 0.44÷0.45=0.98 or by 2%. For a study of this type this is a negligible difference, so it is felt that the laborious, exacting method of factoring in the risk of pregnancy may be omitted in favor of the more simple method.

For comparison with the American figure, the Richland figure for 30-year exposure without factoring in the risk of parenthood is 46 mr×30=1,380 mr=1.4 r. It is therefore about one-third the estimated average of American exposure.[17f] From table 2 the relative importance of the various man-made sources of gonad exposure may be readily compared with the natural radiation and with each other.

Table 2.—*Estimate of Genetically Significant Gonad Exposure from Natural Sources and from Man-made Radiation in Richland, Wash., and United States as a Whole*

Radiation Source of Exposure	Rem per Person, First 30 Years		% of Total	
	Richland	U.S.*	Richland	U.S.*
[illegible]	3.1	3.1	60.0	39.4
[illegible]	1.4	4.1	27.2	52.2
[illegible]	0.5†	0.5	9.7	6.3
[illegible]	0.1‡	0.1‡	1.9	1.3
Occupational	0.06§	0.06§	1.2	0.8
Total	5.16	7.86	100.0	100.0

* Data from National Academy of Science.
† Figures from National Academy of Science, since no radiation therapy is given in Richland and citizens must go elsewhere for this service.
‡ If weapons tests are continued at the same average rate as during the period 1951-1955.
§ Assumption is made that during next 30 years 0.6% of U. S. population will be employed in radiation work and will receive gonad exposures as result of this work, comparable to those of average monitored atomic worker at Hanford Operation, and that this is distributed over the total U. S. population.

Subsequent to the period covered in the study, the hospital has increased the effectiveness of the filters in the primary beam from 1 mm. to 2 mm. equivalent of aluminum, has secured an adjustable diaphragm permitting the use of rectangular fields no larger than necessary to cover the film, has obtained x-ray film which is about 40% more sensitive, and is starting a program for protecting the gonads of males with lead rubber sheet (lead equivalent about 1 mm.) when direct-beam exposures are anticipated.[21] The highest voltage that will permit a satisfactory film contrast is being used.[22] A 1-mm. lead sheet for shielding the testes from the direct beam reduced the dose by factors of 40 to 100 at kilovoltage varying from 74 to 100. To accomplish this, a device (fig. 2) consisting of a small pouch lined with lead sheet, about 1 mm. thick, or equivalent lead rubber and held in place around the male genitalia by suspensory type straps was improvised. A conservative estimate is that these changes will cut the Richland gonad exposure in half.

Because actual figures are used for distribution by age, sex, and anatomic part surveyed and because dosage measurements and estimates are for the actual machine used in most cases, many of the factors which decreased statistical validity in the national studies have been eliminated. However, it must be remembered that dosage is still an estimate, as gonads of both mother and fetus move during pregnancy and time exposure in fluoroscopy must be estimated. In a few procedures, such as those involving the lumbar spine, a small change in the angulation of the x-ray beam may place the gonads just inside or outside the direct beam and change the exposure by a factor of 20 or more.[23] From a national standpoint, the Richland study has the disadvantage that it represents only Richland conditions and is not representative of practices throughout the United States. It is hoped, therefore, that many such studies will be made in order that these may be used by the NAS, or other study groups, to better evaluate the national problem. Such studies will also serve to detect inadequate equipment and local practices and will result in a degree of improvement which may be even more remarkable than that expected in Richland.

Employee Exposure due to Diagnostic Radiology.—The practice of routinely taking x-rays of the backs of all male applicants for employment is an example of the kind of procedure that would result in very appreciable gonad exposures unless the gonads were protected by shielding. Periodic x-rays of the chest add little to gonad exposure, and even this minute exposure could be eliminated by a simple curtain type of shielding if it were considered necessary.[24] They do add to local regional exposure, however. In the phantom study, with use of 14-by-17-in. film, the lung dose was 10 mr per film, while it was 400 mr when the photofluoroscopic technique and a 4-by-5-in. film were used. For this reason, 14-by-17-in. conventional films are used for annual chest x-rays on employees at the Hanford Operation who have potential exposure at work. The male gonad dose during photofluorography (4-by-5-in. film) was 6.7 mr, while it was 0.6 during roentgenography of the chest (14-by-17-in. film). For women, the gonad doses were 3 mr and 3.3 mr respectively.

Considerations in Reducing Exposure in Diagnostic Work

Following the recommendations in Handbook 60[25] on x-ray protection, prepared by the NCRP, will aid greatly in reducing exposure to patients, technicians, and physicians. The most important steps are accurate limiting (coning) and filtering of the primary x-ray beam; use of the most sensitive combination of film, screens, developing chemicals, and temperature; use of the highest voltage that will permit a satisfactory film contrast; and reduction to a minimum of the number of films and screening time of each examination.

Electroluminescense, a new kind of light useful for image intensification, may reduce radiation exposure in fluoroscopy by a factor of 30, when equipment becomes available. Gonads should be protected, when possible, by appropriate screening devices. A qualified expert should assist in planning the structural shielding requirements of any new installation or changes in old installations. He should make a protection survey after completion and at a later date to determine if safety requirements are being met under operating conditions. The expert should also be consulted on the establishment of a monitoring system to determine exposures for each individual for whom there is any reasonable possibility of receiving more than one-fourth the maximum permissible weekly dose.

The various studies, including the Richland, Wash., study, indicate that the greatest care should be taken to minimize gonad exposure during procedures involving the low part of the back and abdomen and the thigh and pelvis, and this becomes even more important during pregnancy.[26] Special care should be taken during examinations of any anatomic portion of infants or small children to avoid, if at all possible, catching the gonads in the primary beam. The patient is so small that the gonads are closer to every area that may be examined. Fluoroscopic examinations of well babies on routine periodic visits to pediatricians should be discouraged or prohibited, according to Stone,[27] because they almost routinely include the gonads in the direct beam and frequently the physician does not know the rate of exposure of the machine. Buschke and Parker,[28] in 1942, and Sonnenblick[29] in 1952, found fluoroscopes with exposure rates varying from 2 to 200 r per minute. If a pelvimetry examination is necessary, in the opinion of the obstetrician, it should be done before pregnancy or late in pregnancy when the fetus is beyond the period of organogenesis and when a comparison can be made of fetal head size to pelvic size.[27]

It seems trite to repeat that x-ray examinations should be limited by careful professional judgment to those required for the health needs of the patient. In summarizing a recent symposium on radiation hazards at the annual meeting of the American Roentgen Ray Society, Chamberlain[30] said, "The present exposure to radiation for medical and dental purposes can be appreciably reduced by techniques and methods that are already available. These are economically feasible, and largely require only interest, education, and the use of well established information and instruments." Interest and education have apparently reached a high point for well-trained radiologists but need to be augmented for the vast number of others who use roentgen ray equipment.

Moeller and associates[31] estimated, in 1953, that there were 125,000 roentgen ray machines in the United States. One-half of these belong to dentists and hospitals, the other half to doctors, osteopaths, chiropodists, and chiropractors. Better understanding is needed on the part of some members of this group in order that they may improve installations and techniques and enhance their judgment in ordering x-rays, which are in the best interest of the patient, after carefully weighing all factors. We should also take the time necessary to explain the pros and cons to the many individuals who have been so alarmed by the frequent discussions which have emphasized the hazards of radiation without explaining the benefits derived. Many do not realize the difference between genetic hazards and somatic hazards or between local and whole-body exposure.

Conclusions

It is hoped that these remarks may have resulted in some improvement in perspective in evaluating the importance of the problem of radiation damage, particularly from a genetic standpoint. A combination of circumstances has tended to emphasize the problem of genetic damage to populations through exposure to radiation. Increasing use of radiation in medicine, industry, and defense has come at a time when genetic experimental evidence indicates that there is no radiation exposure threshold for induction of mutations and that the mutation rate per roentgen exposure is higher than it was thought to be. This has resulted in a need to evaluate genetic hazards to whole populations as well as somatic hazards to individuals. British and American groups have suggested 30 to 80 r as the range within which the dose for doubling the natural mutation rate is likely to be, and the National Committee on Radiation Protection and the National Academy of Sciences (NAS) have recommended a tentative figure of about 10 rem of genetically significant man-made radiation as a reasonable average per capita dose for the future. If human genes have the same response to x-ray exposure as do those of mice, this would be expected to increase the mutation rate by about 20% over a period of many generations.

The NAS estimates the average genetically significant exposure to the American population from diagnostic radiology to be about 4.1 r. A local study in Richland, Wash., just completed, estimated the genetically significant exposure from diagnostic radiology there to be 1.4 r. Improved equipment and techniques instituted after the study are expected to cut this exposure in half with little effort. The genetically significant exposure from natural radiation is considered to be about 3.1 r.[17c]

Local studies have much higher validity for the local area and stimulate local improvements. Many such studies with geographical and installation diversity are needed to give a true picture of the problem at the national level. A plea is made that we each take the trouble to differentiate between the genetic importance of those examinations which involve the gonads in the direct radiation beam, such as the low part of the back and abdomen and the pelvis, and the examinations in which genetic exposure is relatively unimportant, such as those involving the chest, head, and extremities, which make up the vast majority of all x-ray procedures. Simple changes in equipment and techniques, including protection of the male gonads with a lead-lined pouch, may drastically reduce such exposure. Estimates of genetic damage from radiation are based almost strictly on experiments with fruit flies and mice. This must be weighed against the great lengthening in life—19 years during the present century—to which diagnostic radiology has been an important contributor.

If we consider all these points, perhaps we may have our pie and eat it too.

1937 Harris Ave.

Mr. C. M. Unruh made many of the measurements of gonad doses.

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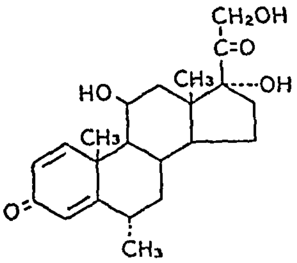
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

Monographs and supplemental statements on drugs described here and in subsequent editions of New and Nonofficial Drugs are based on the evaluation of available scientific data and reports of investigations.

H. D. Kautz, M.D., *Secretary.*

Methylprednisolone. — 6α-Methylprednisolone.—The structural formula of methylprednisolone may be represented as follows:



Actions and Uses.—Methylprednisolone shares the actions and uses of prednisolone, to which it is identical chemically except for the addition of a methyl group at the 6-alpha position. The methyl derivative has an anti-inflammatory potency slightly greater than that of an equal amount of prednisolone; at the same time, it induces somewhat less retention of sodium and water. It is of value for the management of those rheumatic, allergic, dermatological, and ocular disorders known to be responsive to anti-inflammatory glucocorticoids. While not as yet substantiated clinically, it is anticipated that methylprednisolone will ultimately have a place akin to that of other corticosteroids in the temporary control of acute leukemia and other mesenchymal neoplasms, as well as in certain diseases such as nephrosis or ulcerative colitis. The drug is probably not as effective as cortisone or hydrocortisone for the management of acute adrenocortical insufficiency, since it does not exert significant mineralocorticoid activity at the usual doses.

Although methylprednisolone induces somewhat less water and sodium retention than prednisolone, it is capable of producing the same untoward reactions. Peptic ulcer appears to develop rarely in patients receiving methylprednisolone. However, further clinical experience will be necessary to evaluate accurately the incidence of this undesirable side-effect. Hence, all the precautions and contraindications pertinent to the use of prednisolone are applicable to methylprednisolone. (See the general statement on glucocorticoids in New and Nonofficial Drugs.)

Dosage.—Methylprednisolone is administered orally. Dosage should be individualized according to severity of symptoms, degree of response, appearance of side-effects, and anticipated duration of steroid therapy. Because it causes less water and sodium retention than most other glucocorticoids, the usual early sign of overdosage, i. e., a gain in body weight, is not a reliable index of overdosage with methylprednisolone. After relatively high initial doses, the ideal goal of maintenance therapy is to reduce dosage to the lowest possible level compatible with satisfactory clinical response.

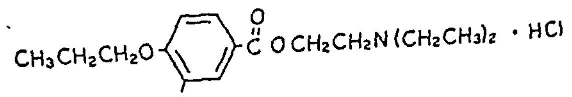
In general, the dosage of methylprednisolone is about two-thirds the required daily dose of prednisolone or prednisone. The drug should be given in four divided doses, preferably after meals and at bedtime. For severe or acute conditions, suppressive doses ranging from 20 to 40 mg. or more per day are given. The suggested dose for acute rheumatic fever is 0.5 mg. per pound of body weight daily until the erythrocyte sedimentation rate has remained normal for one week. For mild or chronic conditions, the initial daily dose ranges from 6 to 20 mg. In chronic diseases, this initial dosage is reduced to maintenance levels by decrements of not more than 2 mg. every seven days. Ultimately, the maintenance dose is usually about one-half the original dose required for the initial control of symptoms.

Preparations: tablets 2 mg. and 4 mg.

Applicable commercial name: Medrol.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of methylprednisolone.

Proparacaine Hydrochloride.—2-Diethylaminoethyl 3-amino-4-propoxybenzoate hydrochloride.—The structural formula of proparacaine hydrochloride may be represented as follows:



Actions and Uses.—Proparacaine hydrochloride is an effective surface anesthetic agent useful in ophthalmology. Although it is a benzoic acid ester, proparacaine is chemically distinct from such other agents as procaine, benoxinate, or tetracaine in that the amino group is in the *meta* rather than in the *para* position. This difference in chemical structure may explain the lack of cross sensitization between proparacaine and other local anesthetic agents.

Proparacaine has an anesthetic potency slightly greater than that of an equal amount of tetracaine. Its onset of action is rapid; surface anesthesia of sufficient intensity to permit tonometry can generally be obtained within about 20 seconds after the instillation of 1 or 2 drops of a 0.5% solution. The duration of such anesthesia is about 15 minutes. Unlike some other topical anesthetics, proparacaine produces little or no initial irritation, stinging, or burning. It does not cause visible hyperemia, lacrimation, increased winking, epithelial drying, or stippling of the cornea, nor does it affect pupillary size. Thus, from the standpoint of onset and duration of action, intensity of anesthesia, and patient-tolerance, proparacaine appears to compare favorably with other agents used as ophthalmic anesthetics.

Proparacaine hydrochloride is useful for most ocular procedures that require topical anesthesia. Among these are tonometry, removal of foreign bodies and sutures, gonioscopy, conjunctival scraping for diagnosis, removal of chalazions from the conjunctival surface, and short operative procedures involving the cornea and conjunctiva. The drug may be used as a surface anesthetic prior to the retrobulbar injection of procaine for intraocular or orbital surgery. Proparacaine has also been employed as the sole anesthetic for cataract extractions and glaucoma surgery. If the drug is instilled at frequent intervals prior to beginning surgery, the depth and duration of anesthesia thus produced may be sufficient to permit these procedures.

Although laboratory studies indicate that proparacaine is too toxic for use as an injection anesthetic, its ophthalmic use has been notably free of side-effects or untoward reactions. To date, there have been few reports of drug sensitivity, either local or systemic. The drug is apparently safe to use in patients who are sensitive to procaine, benoxinate, and tetracaine. Possible deleterious effects or delays in wound healing occasioned by the long-term ophthalmic use of proparacaine are not known but they should be watched for.

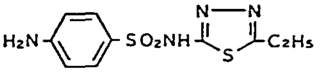
Dosage.—Proparacaine hydrochloride is administered only by topical instillation in the eye as a 0.5% solution. For tonometry, the usual dose is 1 or 2 drops immediately before measurement. For removal of sutures, the instillation of 1 or 2 drops two or three minutes before beginning the procedure is usually adequate; this dose is also used for removal of foreign bodies. When deep anesthesia is required, as in cataract extraction, 1 drop is instilled every 5 to 10 minutes for five to seven doses.

Preparations: solution (topical) 5 mg. per cc.

Applicable commercial name: Ophthaine.

E. R. Squibb & Sons, Division of Olin Mathieson Chemical Corporation, cooperated by furnishing scientific data to aid in the evaluation of proparacaine hydrochloride.

Sulfaethidole.—N^1-(5-Ethyl-1,3,4-thiadiazole-2-yl) sulfanilamide.—The structural formula of sulfaethidole may be represented as follows:



Actions and Uses.—Sulfaethidole is identical in chemical structure to sulfamethizole except that it contains an ethyl rather than a methyl group at the 5 position of the thiadiazole ring. It is, however, a much longer acting drug than sulfamethizole although its spectrum of activity is the same. The drug is useful for the treatment of systemic and urinary tract infections due to organisms sensitive to the bacteriostatic action of sulfonamides. It is readily absorbed from the gastrointestinal tract but does not undergo an appreciable degree of acetylation in the body; about 90 to 95% of the total blood and urine sulfonamide appears as the free form. Both the free and the conjugated forms of sulfaethidole are soluble in urine over a wide pH range. Hematuria, crystalluria, and other indications of renal toxicity have been rarely encountered during therapy with this compound. Because the drug is prepared in a sustained release form, therapeutic blood levels usually can be maintained for a sufficiently long time to necessitate oral administration only once every 12 hours.

The side-effects to be expected with sulfaethidole are the same as with other sulfonamides. However, the incidence of such side-effects—renal, systemic, or dermal—has been much lower. Serious side-effects, such as granulocytopenia and hemolytic anemia, have not been reported to date. Sulfaethidole is contraindicated only in patients with known sulfonamide sensitivity. (See the general statement on sulfonamide compounds in New and Nonofficial Drugs.)

Dosage.—Sulfaethidole is administered orally. The average maintenance dose for adults is 1.3 Gm. every 12 hours. This dose may be increased by one-third (1.95 Gm.) in severe infections, or decreased one-third (650 mg.) for prophylaxis. The average maintenance dose for children is 330 mg. per 25 lb. (11 kg.) of body weight every 12 hours. This dose may be doubled in severe infections or halved for prophylaxis. Initial (priming) doses should be double the maintenance doses.

Preparations: suspension (sustained release, oral) 130 mg. per cc.; tablets (sustained release) 650 mg.

Applicable commercial names: Sul-Spansion, Sul-Spantab.

Smith Kline & French Laboratories cooperated by furnishing scientific data to aid in the evaluation of sulfaethidole.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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POSTGRADUATE MEDICAL EDUCATION AS A MORAL PRECEPT

WHEN THE American Medical Association adopted the brief form of the Principles of Medical Ethics, the responsibility of each physician to continue his own education as well as to add to the sum total of knowledge for the benefit of his patients and the profession was expressed in Principle 2: "Physicians should strive continually to improve medical knowledge and skill, and should make available to their patients and colleagues the benefits of their professional attainments."

Postgraduate or continuation education is a moral as well as an ethical commitment of the medical profession. Enrollment in medical school means more than simply four years of study. It involves a dedicated obligation to a lifetime of active education in view of the prodigious advances in medicine that occur continually. Members of the profession cannot ethically or morally avoid making all possible efforts to learn of the significant advances. Of what help to a sick person is any amount of research that provides means for his more adequate diagnosis or treatment unless his physician knows of this new knowledge? "Each physician must continue to learn in order that others may live."[1] Also, each physician must continue to learn in order to live in peace with himself.

Leaders in medicine have recognized for many years this moral responsibility. A principal reason for the organization of the American Medical Association in 1847 was concern regarding the standards of medical education and medical practice. Scientific sessions have formed a part of the Association meetings since its inception, and scientific exhibits were added to the meetings in 1899. THE JOURNAL was established in 1883. The Council on Medical Education, created in 1904 to replace the Committee on Medical Education first appointed in 1847, has throughout the decades since provided leadership and effective guidance for medical education.

In eras past, when medical advances occurred at a funereal pace easily assimilable by the profession without special effort, informal approaches to continuing education were adequate to the need. In the current setting, physicians require all the assistance they can secure in remaining abreast of scientific developments. Simultaneously with the accelerating pace of basic medical science and clinical advances, the reports of these gains have expanded exponentially so that the individual physician has an appalling problem in attempting to cope with all of the pertinent medical literature. In addition, as the profession has long known, reading alone cannot serve the total objectives of medical education at any level.

While the medical literature, scientific meetings, and day-to-day activities are important in education, as well as for other purposes, regular participation in postgraduate courses is recognized increasingly as an effective means of efficiently continuing medical education. This was accepted by an outside agency two years ago when the Bureau of Internal Revenue of the United States Treasury Department acted to consider such courses as a deductible (hence, a usual and expected) professional expense of physicians.

It is tempting for busy physicians to confuse excuses with valid reasons for nonparticipation in postgraduate medical education. For example, the

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4. Postgraduate Medical Education, in Medical Education in the United States and Canada, J. A. M. A. 165: 1431-1437 (Nov. 16) 1957.

Vollan opinion survey of 1952-1955[2] indicated that distance of physicians from educational centers as well as the problem of no readily available substitute to care for patients were major deterrents to attendance at postgraduate courses even though the profession rated such courses as second only to reading as the preferred educational approach. A recent paper[3] in The Journal indicates that for Kansas, at least, distance of physicians from the University Medical Center had an inverse relationship to the number of physicians participating as well as the number of hours of their course work in three years. Also, there was no correlation between type of practice (solo or group) and the hours spent at postgraduate courses by physicians active in continuing their education. This study of physician performance seems to indicate that distance and patient coverage given as reasons for nonregistration in postgraduate courses may actually have been excuses.

The Council on Medical Education and Hospitals has in the past several years increased its interest and activities in regard to postgraduate medical education. An *ad hoc* Advisory Committee in this field was appointed in 1956, after the conclusion and publication of an extensive three-year survey. A Guide Regarding Objectives and Basic Principles of Postgraduate Medical Education Programs was published in July, 1957, and widely distributed after it was approved by the House of Delegates. The 57th Annual Report on Medical Education in the United States and Canada, prepared by the Council, contained a definitive study of current postgraduate course activities.[4] Studies are now in progress to determine more adequate approaches to the appraisal of the educational merit of the postgraduate courses listed. Another study, geographically oriented, in which 1956-1957 enrollment data are used, will provide information about the mobility of physicians registered in postgraduate courses, to assist in future planning.

In this issue of The Journal, the annual list Postgraduate Courses for Physicians is presented by the Council on Medical Education and Hospitals, based on inquiries earlier this year to all medical schools, many hospitals and medical societies, and other groups in the United States. Although the courses in that list are not evaluated—the list is not a selective one—the information supplied by the sponsors and presented in the list should provide a single reference source that will assist the medical profession in following through with its ethical and moral responsibility for continuing education.

TAX DEDUCTION OF EXPENSES OF POSTGRADUATE EDUCATION

For many years the American Medical Association sought to get the Internal Revenue Service to issue a regulation allowing physicians to deduct their expenditures incurred in postgraduate or continuation education. These efforts were rewarded by the issuance of a proposed regulation two years ago[1] which has now been adopted. The final version of the regulation incorporates several modifications in the proposed regulation, which were suggested by the A. M. A. Law Department. As it now stands the regulation applicable to the deduction of postgraduate educational expenses seems generally fair and equitable.

In essence, a practicing physician may deduct his expenses in taking a postgraduate or special course unless the course is taken with a view to specializing his practice or qualifying for an appointive post. The regulation justifies the deduction of expenses for courses taken in order to maintain the existing kind of practice, as contrasted with those taken for the purpose of beginning specialty practice. If his purpose in taking a course is primarily to keep abreast of new developments so as to maintain his existing practice, the expenses incurred by him are deductible. These expenses include tuition, travel, meals, and lodging.

The time which a physician devotes to continuing education will frequently represent a loss of earnings to him. The fact that he may deduct the cost of this education as a business expense will to some measure reduce the financial loss which he may sustain through the interruption of his practice. The regulation is set forth in full on page 2010 of this issue.

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[1] Tax Deduction Expenses for Education, Medicine and the Law, J.A.M.A. 161:1260-1261 (July 28) 1956.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

ORGANIZATION SECTION

REPORT OF JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

The Joint Commission on Accreditation of Hospitals, 660 N. Rush St., has forwarded the following statement to The Journal.

FOREWORD

The Standards for Hospital Accreditation of the Joint Commission on Accreditation of Hospitals have been formally approved by the Board of Commissioners.

These Standards are considered necessary to insure the quality of medical care in hospitals which the Joint Commission can faithfully recommend to the public. They are not arbitrary or rigid in spirit yet they require general conformity to achieve accreditation by the Commission. To qualify for accreditation the hospital must have at least twenty-five beds, have been in operation at least twelve months and, if located in the United States, be listed in the Administrator's Guide issue of "Hospitals," published by the American Hospital Association.

The Standards are divided into basic principles and methods of procedure. Adherence to the basic principles is essential for the accreditation of all hospitals. The procedures are recommended as guides, dependent upon the type, size, degree of departmentalization, and resources of a particular hospital.

Aware of its responsibilities, the Board of Commissioners is constant in its study of the Standards. Convinced of the essentiality of the basic principles, it is dynamic and realistic in their implementation.

Kenneth B. Babcock, M.D., *Director.*

January 28, 1956

STANDARDS FOR HOSPITAL ACCREDITATION

Basic Principles

The following outlines the basic principles necessary for accreditation of a hospital by the Joint Commission on Accreditation of Hospitals. They are arranged in three sections according to the major functional divisions of a hospital.

I. ADMINISTRATION

Physical Plant—The buildings of the hospital must be constructed and arranged to insure the safety of the patient and promote his welfare.

Governing Body—The governing body has the legal and moral responsibility for the conduct of the hospital as an institution. It is responsible to the patient, the community, and the sponsoring organization. Its official representative is the chief administrative officer of the hospital.

Facilities for the following services are essential:
Dietary
Medical Records
Pharmacy or Drug Room
Clinical Laboratory, and pathological services
Radiology
Medical Library

II. MEDICAL STAFF

The medical staff is responsible to the patient and to the governing body of the hospital for the quality of all medical care rendered to patients in the hospital and for the ethical and professional practices of its members.

III. NURSING

There must be a graduate registered nurse on duty at all times and professional nursing care must be available for all patients at all times.

STANDARDS FOR METHODS OF PROCEDURE

I. ADMINISTRATION

A. Physical Plant

The buildings of the hospital must be solidly constructed with adequate space and safeguards for each patient. Space provided shall not be less than required by existing legal codes. The hospital shall provide:

1. Fire protection by installation of rigid controls and written fire control plans, the elimination of fire hazards, the installation of necessary safeguards such as extinguishers, sprinkling devices, fire barriers, etc., to insure rapid and effective fire control.
2. A sanitary environment to avoid sources and transmission of infections.
3. Facilities for isolation of patients with communicable diseases, especially in obstetrical, newborn, and pediatric sections.
4. Emergency lighting in operating, delivery and emergency rooms, nursery and stairwells.
5. Adequate diagnostic and therapeutic facilities.

B. Governing Body

The governing body is legally and morally responsible for the conduct of the hospital. In the discharge of its duties, it places the responsibility for the medical care of the patient in the hospital primarily upon the medical staff. For effective performance the governing body should do the following:

1. Adopt bylaws in accordance with legal requirements.
2. Meet at regular stated intervals.
3. Appoint committees. There should be an Executive Committee and others as indicated for special purposes.
4. Establish a formal means of liaison with the medical staff preferably by a Joint Conference Committee.
5. Appoint members of the medical staff.
6. Appoint a qualified hospital administrator who is the official representative of the governing body. The administrator is responsible for the conduct of the hospital, and provides liaison among the governing body, the medical staff, the nursing staff, and other departments of the hospital.

C. Essential Services which must be maintained

1. Dietary Department
   a. There shall be an organized department directed by qualified personnel and integrated with other departments of the hospital.

The member organizations of the Joint Commission are the American College of Physicians, the American College of Surgeons, the American Hospital Association, the Canadian Medical Association, and the American Medical Association.

- b. Facilities shall be provided which meet the requirements of the local sanitary code for the storage, preparation, and distribution of food for the general dietary needs of the hospital. These shall include facilities for the preparation of special diets.
- c. There shall be a qualified dietitian on full time or on a consultation basis and in addition, administrative and technical personnel competent in their respective duties.
- d. There shall be a systematic record of diets, correlated with the medical records.
- e. Departmental and interdepartmental conferences shall be held periodically.

2. *Medical Record Department*
   - a. Administrative Responsibilities
     - 1) There shall be a medical record maintained on every patient admitted for care in the hospital.
     - 2) Records shall be kept inviolate and preserved for a period of time not less than that determined by the Statute of Limitations in the respective state.
     - 3) Qualified personnel adequate to supervise and conduct the department shall be provided.
     - 4) A system of identification and filing to insure the rapid location of a patient's medical record shall be maintained. The unit number system is suggested; however, a serial number system or modification of this is acceptable.
     - 5) Records should be indexed according to disease, operation, and physician and should be kept up-to-date.
     - 6) All clinical information pertaining to a patient should be centralized in the patient's record.
     - 7) The Standard Nomenclature should be used as a nomenclature and is preferred if medical records are coded.
   - b. Medical Staff Responsibilities
     - 1) The medical record must contain sufficient information to justify the diagnosis and warrant the treatment and end-results.
     - 2) Only physicians and members of the house staff are competent to write or dictate medical histories and physical examinations.
     - 3) Current records and those on discharged patients should be completed promptly.
     - 4) Records must be authenticated and signed by the physician.
   - c. The medical record should contain the following information:
     - 1) Identification data
     - 2) Complaint
     - 3) Present illness
     - 4) Past history
     - 5) Family history
     - 6) Physical examination
     - 7) Consultations
     - 8) Clinical laboratory reports
     - 9) X-ray reports
     - 10) Provisional diagnosis
     - 11) Tissue report
     - 12) Treatment: medical and surgical
     - 13) Progress notes
     - 14) Final diagnosis
     - 15) Summary
     - 16) Autopsy findings

3. *Pharmacy or Drug Room*
   - a. There shall be a pharmacy directed by a registered pharmacist or drug room under competent supervision.
   - b. Facilities shall be provided for the storage, safeguarding, preparation, and dispensing of drugs.
   - c. Personnel competent in their respective duties shall be provided in keeping with the size and activity of the department.
   - d. Records shall be kept of the transactions of the pharmacy, and correlated with other hospital records where indicated. Such special records shall be kept as are required by law.
   - e. Drugs dispensed shall meet the standards established by the United States Pharmacopeia, National Formulary, New and Nonofficial Remedies, British Pharmacopeia, or Canadian Formulary.
   - f. There should be an automatic stop order on dangerous drugs.

4. *Laboratories*
   - a. Clinical
     - 1) A clinical laboratory adequate for the individual hospital must be maintained in the hospital.
     - 2) Provision shall be made to carry out chemical, bacteriological, and serologic examinations.
     - 3) Facilities should be available at all times.
     - 4) Personnel adequate to supervise and conduct the service should be provided.
     - 5) Urinalysis and at least a hemoglobin or hematocrit should be routine examinations on all admissions.
     - 6) Signed reports should be filed with the patient's record and duplicate copies kept in the department.
   - b. Pathological
     - 1) The services of a pathologist must be provided as indicated by the needs of the hospital.
     - 2) All tissues removed at operation should be sent for examination. The extent of the examination should be determined by the pathology department.
     - 3) Signed reports of tissue examinations should be filed with the patient's record and duplicate copies kept in the department.
     - 4) Tissue reports should be indexed according to pathologic diagnosis.
   - c. Blood Bank

     Facilities for procurement and safe-keeping of blood should be provided or readily available.

5. *Radiology*
   - a. The hospital must maintain radiologic services according to the needs of the hospital.
   - b. The radiology department shall be free of hazards for patients and personnel.
   - c. The interpretation of radiologic examinations shall be made by physicians competent in the field.
   - d. Signed reports should be filed with the patient's record and duplicate copies kept in the department.
   - e. Reports should be indexed according to radiologic diagnosis.

6. *Medical Library*
   - a. The hospital must maintain a medical reference library according to the needs of the hospital.
   - b. Facilities should be provided to meet the requirements of the services in the hospital.
   - c. Basic textbooks and current periodicals should be available and catalogued according to the needs of the hospital.
   - d. Personnel should be provided to assure efficient service to the medical staff.

D. Services which may be maintained

1. *Medical Social Service Department.* If a department is maintained:
   - a. There shall be an organized department directed by a qualified medical social service worker, and integrated with other departments of the hospital.

b. Facilities shall be provided which are adequate for the personnel of the department, easily accessible to patients and to the medical staff, and which assure privacy for interviews.

c. Records of case work shall be kept. Such records shall be available only to the professional personnel concerned.

d. Departmental and interdepartmental conferences shall be held periodically.

2. *Emergency Service.* If a service is maintained:

a. There shall be a well organized department directed by qualified personnel and integrated with other departments of the hospital.

b. Facilities shall be provided to assure prompt diagnosis and emergency treatment.

c. There shall be adequate medical and nursing personnel available at all times.

d. Adequate medical records on every patient must be kept.

e. There shall be a written plan for the care of mass casualties and this plan should be coordinated with the inpatient and outpatient services of the hospital.

II. MEDICAL STAFF

A. Responsibilities

The governing body of the hospital must obviously delegate the responsibility of medical functions to the medical staff, including recommendations as to the professional qualifications of all who practice in the hospital. The medical staff is responsible for the quality of medical care rendered to patients in the hospital. Maintaining high standards of medical care will depend upon the character of the staff and the effectiveness of its organization to carry out the following duties:

1. Selection of those recommended for staff appointments and hospital privileges.
2. Constant analysis and review of the clinical work done in the hospital.
3. Support of medical staff and hospital policies.
4. Maintenance of adequate medical records.
5. Procurement of autopsies (a minimum of 20 to 25% of hospital deaths).
6. Holding of necessary consultations. Except in emergency, consultation with another qualified physician shall be required in all first Cesarean sections and in all curettages or other procedures by which a known or suspected pregnancy may be interrupted. The same requirement shall apply to operations performed for the sole purpose of sterilization on both male and female patients. Included in consultations required under this Standard are all those which are required under the rules of the hospital staff. In major surgical cases in which the patient is not a good risk, and in all cases in which the diagnosis is obscure, or when there is doubt as to the best therapeutic measures to be utilized, consultation is appropriate. Obviously, judgment as to the serious nature of the illness and the question of doubt as to diagnosis and treatment rests with the physician responsible for the care of the patient. It is the duty of the hospital staff through its chiefs of service and Executive Committee to see that members of the staff do not fail in the matter of calling consultants as needed. A consultant must be well qualified to give an opinion in the field in which his opinion is sought. A satisfactory consultation includes examination of the patient and the record and a written opinion signed by the consultant which is made part of the record. When operative procedures are involved, the consultation note, except in emergency, shall be recorded prior to operation.

B. Membership

1. *Appointment*

a. Procedure

Staff appointments are made officially by the governing body. Recommendations are customarily made by the active staff, and in no case should a governing body make an appointment to the staff without such a recommendation.

b. Qualifications

Members of the staff must be qualified legally, professionally, and ethically for the positions to which they are appointed.

c. Tenure

Limited terms of appointment are preferred but not required. The prevailing custom is for a term of one year, with reappointments continued as long as qualifications remain satisfactory.

2. *Categories*

The privileges of each member of the medical staff shall be determined on the basis of professional qualifications and demonstrated ability.

a. Active Staff

Regardless of any other categories having privileges in the hospital, there shall be an active staff, properly organized, which shall perform all the organizational duties pertaining to the medical staff. These shall include:

1) Maintenance of the proper quality of all medical care and treatment in the hospital.

2) Organization of the medical staff, including adoption of rules and regulations for its government (which require the approval of the governing body), election of its officers, and recommendations to the governing body upon all appointments to the staff and grants of hospital privileges.

3) Other recommendations to the governing body upon matters within the purview of the medical staff.

b. Other Categories of the Staff

In larger hospitals, and in some smaller hospitals, the medical staff may include one or more of the following categories in addition to the Active Staff, but this in no wise modifies the duties and responsibilities of the Active Staff.

1) Honorary Staff

The Honorary Staff shall be former Active Staff, retired or emeritus, and other physicians of reputation whom it is desired to honor.

2) Consulting Staff

The Consulting Staff shall be recognized specialists willing to serve in such capacity. A member of the Consulting Staff may also be a member of the Active Staff, but only if the two appointments are made.

3) Associate Staff

The Associate Staff shall be those members who use the hospital infrequently or those less experienced members undergoing a period of probation before being considered for appointment to the Active Staff.

4) Courtesy Staff

The Courtesy Staff shall be those who desire to attend patients in the hospital but who, for some reason not disqualifying, are ineligible for appointment in another category of the staff.

5) Privileges of the Hospital

Privileges of the hospital may be extended to other qualified physicians under the same conditions as apply to the Courtesy Staff.

C Organization

1 *Officers*

There shall be a President or Chief of Staff, a Vice-President or Vice-Chief, a Secretary, and such other officers as may be necessary for the government of the staff These officers shall come from the Active Staff and shall be elected by the Active Staff, unless this is precluded by hospital organization

2 *Bylaws*

Bylaws conforming to the principles expressed by the Joint Commission on Accreditation of Hospitals shall govern the staff

3 *Committees*

The complexity of committee organization depends upon the size and composition of the medical staff of the individual hospital A small staff may wish to function as a committee of the whole Others may wish to combine committee functions in two or three committees The structure of committee organization is a decision to be made by the medical staff so long as the following required committee functions are carried out

a Executive Committee

The Executive Committee shall co-ordinate the activities and general policies of the various departments, act for the staff as a whole under such limitations as may be imposed by the staff, and receive and act upon the reports of the Medical Records, Tissue and such other Committees as the medical staff may designate The Executive Committee shall meet at least once a month and maintain a permanent record of its proceedings and actions

b Qualifications or Credentials Committee

The Qualifications or Credentials Committee shall review applications for appointment and reappointment to all categories of the staff They shall delineate the privileges to be extended to the applicant and make appropriate recommendations to the staff

c Joint Conference Committee

The medical staff members of the Joint Conference Committee shall represent the staff in meetings with the governing body of the hospital or a committee of that body This Committee shall be a medicoadministrative liaison committee and the official point of contact among the medical staff, the governing body, and the administrator

d Medical Records Committee

The Medical Records Committee shall supervise and appraise the quality of medical records, and shall insure their maintenance at the required standard The Committee shall meet at least once a month and submit to the Executive Committee a report in writing which will be made a part of the permanent record

e Tissue Committee

The Tissue Committee shall study and report to the staff, or to the Executive Committee of the staff, on the agreement or disagreement among the preoperative, postoperative, and pathological diagnoses and on whether the surgical procedures undertaken in the hospital were justified or not This study will also include those procedures in which no tissue was removed The report to the Executive Committee shall be in writing on at least a monthly basis

4 *Staff Meetings*

The sole objective of staff meetings is improvement in the care and treatment of patients in the hospital This is facilitated by a thorough review and analysis of the clinical work done in the hospital on at least a monthly basis

a There are three patterns for medical staff meetings which will accomplish this purpose

1) Monthly meetings of the active staff, not less than twelve in each calendar year.

2) In well organized and departmentalized hospitals, departmental conferences and clinicopathologic conferences may be substituted for meetings of the entire staff, provided that an adequate review of the clinical work done in the hospital is covered by one or another of such conferences, and further provided that at least one meeting of the entire Active Staff is held during each quarter of the year. At such meetings a report of the review of the medical work of the hospital must be presented by the Executive Committee In very large hospitals where attendance requirements are obviously met by departmental meetings and where physical facilities are not available for large audiences, the Commission may accept departmental meetings in lieu of meetings of the entire medical staff.

3) In hospitals where adequate review of the medical work in the hospital is carried out by the Medical Records and Tissue Committees, and appropriate study and action is taken by the Executive Committee on not less than a monthly basis, one meeting of the entire Active Staff must be held during each quarter of the year At such meetings a report of the medical work of the hospital must be presented by the Executive Committee

b Active Staff attendance shall average at each meeting at least 50% of the active staff who are not excused by the Executive Committee for just cause Each active staff member shall attend 50% of staff meetings unless excused by the Executive Committee for just cause

c In addition to matters of organization, the programs of such meetings must include a report of the Executive Committee and be limited largely to the review of current or recent cases in the hospital Scientific programs not associated with the work of the hospital do not meet this requirement.

d Business or other executive sessions of the staff shall be conducted by the Active Staff and other categories of the staff may be excluded

e Adequate minutes of all meetings shall be kept.

D Departmentalization

Division of the staff into services or departments to fulfill medical staff responsibilities promotes efficiency and is recommended in general hospitals with 75 or more beds Functional division of the medical staff into more than the minimal medical and surgical services is frequently desirable in larger hospitals It is necessary that each autonomous service or department be organized and function as a unit The following are considered minimal.

1 *Personnel*

Personnel of each service or department shall be qualified by training and demonstrated competence, and shall be granted privileges commensurate with their individual abilities

2 *Chief of Service or Department*

The chief of service or department shall be the member of the service or department best qualified by training and experience, and demonstrated ability for the position He shall be responsible for the general character of the professional care of the patients on his service or department, and make recommendations as to qualifications of its members His duties shall also include recommendation to the administrator as to the procurement of drugs, supplies, instruments, and equipment to insure maximum benefit to the patient Additional duties of the chief of service or department shall include the following:

   a. Surgical—recommendations as to sterile procedures and operating room policies.
   b. Obstetric.
      1) Supervision of care of newborn, if there is no organized service responsible for the nursery;
      2) Recommendations as to sterile procedures and delivery room policies.
   c. Clinical Laboratory.
      1) Participation in staff and departmental meetings;
      2) Reporting upon all specimens examined, and maintaining a duplicate file of these reports in the department. This includes all tissues removed in the hospital.
   d. X-ray Department
      1) Participation in staff and departmental meetings;
      2) Reporting upon all examinations and treatments, maintaining a duplicate file of these reports in the department;
      3) Insuring that safety precautions as to radiation and fire are observed strictly.

3. *Conferences*

Each service or department should have frequent, periodic conferences, attended by all its members, to consider clinical and organizational problems peculiar to the service. Records of these meetings shall be kept, become part of the records of the medical staff, and be available for inspection.

E. Departments which may be maintained

1. *Anesthesia*

The organization of the Department of Anesthesia shall be comparable to that of the other services of the medical staff. In addition, there shall be required in every case:

   a. Preanesthetic physical examination with findings recorded;
   b. Anesthetic record on special form;
   c. Postanesthetic follow-up, with findings recorded.

2. *General Practice Department*

A Department of General Practice shall be an organized segment of the medical staff comparable to that of other staff departments with the following modifications:

   a. The responsibilities of this department shall be limited to administration and education. It shall not be a clinical service and no patients shall be admitted to the department. If and when desirable, however, the department may be made responsible for conducting the outpatient clinic in whole or in part.
   b. Since the Department of General Practice will not have a separate service, the members of the General Practice Department shall have privileges in the clinical services of the other departments in accord with their experience and training, on recommendation of the Credentials Committee. In any service in which any general practitioner shall have privileges, he shall be subject to the rules of that service and subject to the jurisdiction of the chief of the clinical service involved.
   c. The medical staff should give to the General Practice Department such administrative responsibilities in the conduct of medical affairs as are desirable to meet the needs of the hospital.

3. *Rehabilitation Department*

The organization of the Rehabilitation Department shall be comparable to that of other departments of the hospital.

4. *Outpatient Department*

The Outpatient Department shall be organized into sections (clinics) the number of which shall depend on the degree of departmentalization of the medical staff, available facilities, and the needs of the community.

   a. Organization and Personnel

   There shall be such professional and nonprofessional personnel as are required for efficient operation.

   b. Facilities

   Facilities shall be provided to assure the efficient operation of the department.

   c. Medical Records

   Medical records shall be maintained, and correlated with other hospital medical records.

   d. Conferences

   Conferences, both departmental and interdepartmental, shall be conducted to maintain close liaison between the various sections within the department and with other hospital services.

5. *Dental*

The dental staff shall conform in general to standards established for the medical staff. In addition:

   a. Members of the dental staff must be qualified legally, professionally, and ethically for the positions to which they are appointed.
   b. Patients admitted for dental services shall be admitted on a surgical service and shall be the responsibility of the chief of that service.
   c. Adequate medical survey by a member of the medical staff shall be done on each patient before dental surgery. Indicated consultations shall be held in complicated cases.

III. NURSING DEPARTMENT

Adequate care of the hospital patient requires well-organized and efficient nursing. All hospitals must meet the following requirements for accreditation:

A. Functions and Responsibilities

Nursing care for all patients is a primary responsibility of the nursing department, which must function in close relationship with other services of the hospital, both administrative and professional. This requires the establishment of a departmental plan of administrative authority with a definite outline of responsibilities and duties for each category of nursing personnel. This shall deal not only with patient care, but also with the educational responsibilities of the nursing department. Adequate nursing service must also be provided for the surgical suite, delivery rooms, clinics and other services of the hospital in keeping with the size and degree of activity.

B. Personnel

Personnel engaged for administrative or professional duties must be qualified by training and experience, and demonstrated ability for their assignments. All hospitals must provide nursing personnel to meet the following minimum requirements:

1. Director of department.
2. Assistant to the director for evening and night services.
3. Department or floor supervisors.
4. An adequate number of professional nurses and ancillary personnel for bedside care.

Nurses assigned to care for obstetric patients and the newborn must not have other duties which may create danger of infection being carried to this service.

C. Records

Adequate records shall be maintained.

D. Departmental Meetings and Conferences

Meetings of the nursing staff, or of each department staff, shall be held at least monthly for discussion of nursing problems related to care of patients and administration.

HEARINGS BEFORE CONGRESS ON VETERANS CARE

June 18, 1958

Honorable Olin E. Teague
Chairman, Committee on Veterans' Affairs
U. S. House of Representatives
Washington 25, D. C.

Dear Congressman Teague:

In connection with the current hearings of your Committee concerning Veterans compensation legislation, I would like to take this opportunity to restate the position of the American Medical Association on certain of the principles involved.

Our position with respect to the provision, by the Federal Government, of medical care and hospitalization for veterans was last restated by our House of Delegates in 1956. The Association recommends that:

1. Medical care and hospitalization be supplied by the Federal Government to those veterans who have physical or mental diseases or disabilities which were incurred or aggravated as a result of military service; and
2. Medical care and hospitalization would not be provided for veterans with non-service-connected diseases and disabilities.

The American Medical Association is and always has been in complete agreement that the Federal Government has the duty to care for any man who has become physically or mentally diseased or disabled as a result of military service. We believe, however, that the provision of medical care and hospitalization for veterans with non-service-connected disabilities by the Federal Government is unsound. Therefore, we are opposed to the existing law as well as to any bills which would continue to extend the provision of medical care by the Federal Government for veterans with non-service-connected diseases and disabilities.

We also note that there are a number of bills, now pending before the Veterans Affairs Committee, which would establish a presumption of service-connection for a large variety of diseases and conditions or extend the period of years which previously recognized presumptions of service-connection would operate. We have always been opposed to the determination of service-connection of diseases and disabilities by legislative enactment. We believe that the question of whether a given disease in a given individual, is a result of or was aggravated by military service, can only be properly answered on the basis of the facts of the individual case. There are many factors which must be determined and weighed on the basis of the actual case history of the individual before service-connection can be accurately determined.

It is our belief that the only true mission of Veterans Administration's Department of Medicine and Surgery, is to provide medical care for veterans with service-connected ills. Nevertheless, as long as non-service-connected cases are legally eligible under the present laws, we believe that every effort must be made to insure that service-connected cases, which have now dwindled to a mere 15% of annual hospital admissions, do not become relegated to the background of the VA hospital picture.

I would appreciate it if this letter were made a part of the record of the current hearings.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

Reproduced below is the statement of the American Medical Association before the Senate Committee on Armed Services relative to reorganization of the Department of Defense. Testimony was presented by Dr. Richard L. Meiling on June 26, 1958.

Mr. Chairman and Members of the Committee:

My name is Richard L. Meiling. I am Chairman of the Committee on Military Medical Affairs and a member of the Council on National Defense of the American Medical Association. I am a practicing physician in Columbus, Ohio, and Associate Dean of the College of Medicine of Ohio State University.

In 1948, I served as Medical advisor to the Committee on the National Security Establishment of the first Hoover Commission. Later, I served as a member of the Armed Forces Medical Advisory Council to the Secretary of Defense; and from 1949 to 1951, was Director of Medical Services, Chairman of the Armed Forces Medical Policy Council and the Assistant to the Secretary of Defense for Medical and Health Affairs. From 1951 to 1953, I served as a consultant to the Secretary of Defense.

I appear today on behalf of the American Medical Association. Our statement concerning the "President's Defense Reorganization Plan" will be limited to a discussion of the need for maintaining the position and office of "The Assistant Secretary of Defense (Health and Medical)" within the Department of Defense. H. R. 12541, as passed by the House of Representatives, as well as S. 3544, and the President's Reorganization Plan, makes no provision for retaining this office and position.

Our Association has demonstrated for more than a century its interest in assuring that the best available medical services are provided for our Armed Forces in time of war and peace. Since the enactment of the National Security Act of 1947, the Association has been instrumental in presenting, to both the Legislative and Executive branches of the Government, our recommendations concerning the need for health and medical policy coordination at the highest level of our Government.

In 1948, the first Hoover Commission recommended that, to be effective, control over military medical policy should be exercised at the level of the Secretary of Defense. The first step in this direction was taken in July 1949 by administrative action of the Secretary of Defense. In 1953, the Rockefeller Committee on the Department of Defense Organization, recognizing that stronger medical direction was needed, stated that the position of Assistant Secretary of Defense (Health and Medical) was justified and necessary to provide adequate staff assistance in the field of medicine and health to the Secretary of Defense. Reorganization Plan no. 6, which was prepared as a result of this recommendation and which was adopted in 1953, provided for establishing this position. In 1955, the Hoover Commission recommended still further strengthening of the position of the Assistant Secretary of Defense (Health and Medical).

The revolutionary changes that have taken place in the technique and weapons of war have drastically accelerated the scale and tempo of military destructiveness. These developments have, at the same time, increased the compelling need for a unified medical and health policy and program control throughout the administrative and command structure of the defense establishment.

Since the establishment in 1949 in the Office of the Secretary of Defense of a unified policy control of the military medical services, the United States Armed Forces have experienced the lowest case fatality rate of any period in peace and in war.

At the same time, the military medical services have maintained the highest effective rate while American Armed Forces were serving in disease-ridden areas throughout the world and under some of the most hazardous conditions. It was the military medical services which established the precedent for a unified, military supply procurement agency. It was through their efforts that a "single" supply catalog was set up. The Department of Defense blood program for supplying whole blood for our overseas command was established during the Korean campaign.

Economy and efficiency have been established by joint utilization of military medical facilities, military medical logistics, intelligence and operation, and patient evacuation and transportation. This cooperation has also proved effective in the field of research, scientific development and in educational and professional programs. All this has been under the policy and program control of the Assistant Secretary of Defense (Health and Medical) and his predecessors in the office of the Secretary of Defense.

During the Korean conflict, this office directed the coordination of medical and health liaison with the forces of the United Nations, a program which has been continued with NATO and SEATO forces. During this same period, this office established the first governmental inter-agency medical council responsible for the coordination of medical efforts on behalf of our wartime and peacetime health and medical care missions.

These past nine years of experience have clearly demonstrated the need and effectiveness of the Assistant Secretary of Defense (Health and Medical) in the formulation of military medical policy and programs throughout all echelons of the Department of Defense. At the same time, the incumbent of this position, because of its rank, has commanded the respect of his opposite numbers in the highest circles in our own government, foreign governments, and in the professional and scientific organizations.

It is the considered opinion of the American Medical Association that to abolish or downgrade the position of the Assistant Secretary of Defense (Health and Medical) would have a most deleterious effect at all echelons within the defense organization upon the medical and health services of our Armed Forces and upon the morale of military personnel. This effect would involve the morale of personnel, as well as medical and health policies and programs, at all echelons of the defense organization. In addition to eliminating a central agency within the Department of Defense for dealing with military health problems, the abolishment or downgrading of this office would be reflected in the inter-agency health programs within our own government and in the medical and health relationships between our government and the other governments with whom we are allied.

We believe, therefore, that it is in the best interests of the Armed Forces, the military medical and health services, and our country, that the position of the Assistant Secretary of Defense (Health and Medical) be maintained in the Department of Defense with a civilian physician appointed to this position.

It is our specific recommendation, therefore, that the bill be amended by the addition of this provision: "One Assistant Secretary shall perform such duties and exercise such power as the Secretary of Defense may prescribe in the field of health and medicine." May I thank you on behalf of the American Medical Association for your attention and assure you of the Association's desire to cooperate and assist in every way possible on matters relating to our national security, the military medical services and the provision of the best possible health services to the personnel of the Armed Forces.

Reproduced below are statements of the American Medical Association before the Committee on Ways and Means relative to amendments to the Social Security Act. Testimony was presented by Drs. Leonard Larson and Frank H. Krusen on June 27, 1958.

Dr. Larson: I am Dr. Leonard Larson of Bismarck, North Dakota.

I am appearing here . . . as the representative of the Board of Trustees of the American Medical Association, with Dr. Frank H. Krusen of Rochester, Minnesota, to discuss with you the views of the medical profession concerning certain of the provisions of H. R. 9467, 85th Congress, and other similar bills. In accordance with the instructions included in your release of May 29, we are limiting our testimony to matters which are of primary interest to the medical profession. We may, however, request permission later to submit a written statement, for the record; outlining our position on the other bills before your Committee dealing with the Social Security program.

Before calling on Dr. Krusen, I would like to discuss the general attitude of the medical profession regarding proposals such as H. R. 9467 and to briefly review with you some of the more important recent medical advances under our present system of medical care.

In 1949, when legislation providing for a program of national compulsory health insurance was pending before Congress, we strongly opposed it. It was thereafter clearly rejected by the Congress, and the American people. Today, you have before you proposals which would authorize service benefits in the form of hospitalization and surgical care for the retired and survivor beneficiaries under Title II of the Social Security Act. Such a proposal would mean a federally financed and federally controlled system of medical and hospital care, first for Social Security beneficiaries, subsequently for other groups and ultimately for everyone.

The medical profession has been and is still acutely aware of the existence of medical care problems among the aged. We agree that efforts to solve these problems should be continued and increased. We do not agree, however, with the advocates of the pending legislation, as to the nature and extent of the problems, or as to the means of solving them. We feel, as do many others, that traditional voluntary private methods can eliminate existing deficiencies and at the same time preserve individual and community freedom.

In reviewing the progress which has been made through the private enterprise approach it is evident that federal intervention is not required. I shall not outline the impressive record which has been established by the private health insurance industry and by the Blue Shield and Blue Cross plans. Representatives of these agencies have presented their own statements in this regard. I would like, however, to comment very briefly about medical progress in general.

The advances of medical science since the beginning of the twentieth century offer convincing evidence of what can be done when competent medical researchers and practitioners have an opportunity to work with complete freedom. A review of the medical discoveries since the turn of the century would require volumes. Drugs and operations, for example, alone could provide endless material for discussion of the forward march of medicine. Insulin, vitamins, sulfanomides, penicillin and other antibiotics are only a few of the outstanding discoveries in the drug field. Isotopes and betatrons have become part of the medical language. Entirely new approaches to illness have been discovered, as a result of which the full possibilities of what were practically unknown subjects such as physical medicine and rehabilitation, are now being explored with a thoroughness that offers much promise for the future.

The decline in the general mortality rate from 17.2 deaths per 1,000 population in 1900 to only 9.6 in 1957 underscores the health progress which has been made. While the population has doubled in this period, the number of persons over 65 years of age has quadrupled and a significant gain in life expectancy, even in late middle age, has resulted from the mortality reduction. Life expectancy at birth in 1900 was estimated at 47.3 years; in 1955 it was estimated at 70.0 years.

Thus, we in medicine have helped to create not only the problems of the aged, we have helped to create the aged. We have done it under the free choice system. We can solve the problems in the same way.

The American Medical Association has, throughout its history, been a champion of sound progress in medicine. It has had to fight many battles against quackery, against improper interference and against slipshod medical training and practice. As an association, we will continue to support all programs for the good of the health of the public, as we have done over the years. It is our conviction, however, that the medical provisions of H. R. 9467 are unwise, unnecessary and not in the public interest.

In addition to the points which Dr. Krusen will present, let me point out that no one knows what this proposed program would cost. It is our best estimate that initially it would run about two billion dollars per year. What it would cost eventually cannot be estimated. But we do know historically that the cost of programs such as this one is invariably much higher than the amount initially predicted for them—witness the financial plight of socialized medicine in England.

This tremendous and unpredictable drain on the Social Security Trust Fund could seriously jeopardize the actuarial soundness of the entire program. The retirement funds of millions of Americans would be endangered through the launching of a program of this type at a time when the Social Security system, for the first time in history, is receiving less income than is being paid out.

The proposal also departs from the best thinking of social insurance experts who agree that the original "floor-of-protection" concept of the Social Security Act should not be violated. Up to now, the principle of Social Security has been one of cash payments to insured persons who are disabled or retired or to their survivors. The pending proposals would graft on to this cash benefit system a health service program.

The members of the medical profession, as citizens and as physicians, look with suspicion and fear upon legislation, such as H. R. 9467 which, in our opinion, would stifle and destroy the energetic and imaginative free-enterprise medical programs now in progress. A proposal which would legislate the aged into a permanent state of dependency and most important one that would propel us completely and irresponsibly into a federally controlled health care program.

With your permission, Mr. Chairman, I would like to call on Dr. Krusen to present additional views with respect to H. R. 9467.

Dr. Krusen: As Dr. Larson has stated, the primary interest of the American Medical Association in the Social Security legislation pending before this Committee is related to H. R. 9467 and similar bills.

Before identifying and discussing the provisions of these proposals, I would like to state that the medical profession has not in the past, and is not now, taking a position in opposition to the over-all Social Security program. The American Medical Association did not oppose the passage of the Social Security Act in 1935 or subsequent amendments which adhered to its original basic character as a "floor-of-protection" cash benefit program. However, H. R. 9467, 85th Congress and other recent proposals, which would introduce disability and health service benefits into the Old Age, Survivors and Disability Insurance structure, represent, in our opinion, a major and dangerous deviation from the original concept of the system.

H. R. 9467, if enacted, would authorize a federally subsidized and controlled system of hospital, surgical, nursing home and dental care, irrespective of need, for between 12 and 13 million eligible Social Security beneficiaries. This entire program would be under the direction and control of the Department of Health, Education and Welfare and would be financed, in part, by an increase in Social Security taxes.

Hospital care, including drugs, appliances and services customarily furnished by a hospital, such as bed and board, nursing care, laboratory services, and ambulance services would be available, subject to administrative regulations, in those hospitals that enter into a written agreement with the administering agency. Eligible nursing homes would be those where "skilled nursing care" could be obtained, provided a written agreement was negotiated with the government. Physicians recognized by the bill as qualified to perform non-elective surgery would be limited to those certified by the American Board of Surgery or members of the American College of Surgeons. Hospitals, nursing homes and physicians would all be required to accept, in full payment for facilities and services, charges and fees established by the Secretary of the Department of Health, Education and Welfare.

Before commenting in general on the medical problems of the aged, I would like to outline for the Committee some of the more specific reactions which the medical profession has to H. R. 9467. First of all, let me say that, in our opinion, this legislation would inevitably result in poorer—not better—health care for the intended beneficiaries.

Because of the relatively recent emergence of this problem, no one in this country has at this time sufficient information on the health needs of the aged on which to base authoritatively such a drastic, far-reaching proposal. However, some of the things we do know are that the aged, for the most part, do not need short stays in general hospitals but rather improved home and community care as well as less costly and improved chronic illness and nursing home facilities. We also know that the medical needs of the aged are primarily non-surgical and that the surgical care now being provided is supplied primarily by physicians who are not Board Certified and who are not members of the American College of Surgeons.

However, the most serious aspect of this legislation is that it is National Compulsory Health Insurance all over again. Under this proposal, the federal government would finance the health care of from 12 to 13 million citizens through earmarked compulsory taxes; the government would control the disbursement of funds; the government would determine the benefits to be provided; the government would set the rates of compensation for hospitals, nursing homes and physicians; the government would audit and control the records of hospitals, nursing homes and patients; and the government would promulgate and enforce standards of hospital and medical care.

Under this proposal the beneficiaries would be restricted in their choice of hospital and physician. Only selected physicians and those hospitals and nursing homes entering into agreements with the

Federal government would participate. Inasmuch as many highly qualified hospitals and doctors would prefer to remain independent of government control, even if eligible to participate, there would be a limitation in the number of physicians and medical facilities available.

The professional relationship between the doctor and his patient would be hampered. Government regulations would be imposed on patient and physician alike, bringing a third party between them. Required conformance to administrative regulations could also hamper the physician from prescribing treatment which, in his professional opinion, is indicated.

The hospitalization provisions of the proposal would create a needless and dangerous overcrowding of already hospital facilities. With personal and family financial responsibility eliminated, many aged persons would seek unnecessary hospital and medical care for trivial and imaginary illnesses and would become unduly concerned with their health. In other countries where similar legislation is in effect, there has been a staggering increase in the use of hospital facilities by the aged.

The bill also says, in effect, "The aged cannot obtain voluntary health insurance protection." This is not factual, since more than 40% of the aged presently have some form of voluntary health insurance. These figures are particularly significant when you realize that only 20% were covered as recently as 1950. This rate of progress shows that the problem is being solved by the health insurance industry which is steadily gaining a vast experience in this relatively new field of medical and hospital insurance. H. R. 9467 would destroy the voluntary health insurance business among the aged group and could eventually, we feel, destroy the entire voluntary private health insurance movement, which now covers some 123,000 Americans.

Inasmuch as this legislation primarily concerns persons in the older age group, I would like to comment on the nature of their medical care problems and what the medical profession and other health groups are doing in their behalf.

In the last quarter century the population aged 65 and over in the United States has increased until it now numbers between 14 and 15 million persons. This increase in numbers, plus a marked visible variation in the effect of aging, has stimulated the investigation of numerous complex medical and related questions. We are inclined to believe as a result of our studies to date that the lack of preparation for advanced age and the impact of environment are the real causes of degeneration which were formerly attributed to the mere passage of years.

What we should understand is that the solution to these problems will require the effort of many segments of our society in addition to the medical profession. Passage of a law will not wipe out these problems, which are of concern to all of us.

Many of the ills of the aged are the direct result of the inferior role in which this group has been placed. Their experience, wisdom and know-how are being wasted and the resulting lack of meaningful activity has led to emotional frustration and physical breakdown.

This is a trend which has numerous dangerous implications. Basically the problem calls for aggressive leadership at the family and community level to help bring these millions of potentially useful citizens back to their rightful place in society and to give their lives purpose and dignity.

As physicians there is one thing about which we are certain—whether we are dealing with older persons or with any age group of the population—the first fundamental of good medicine is to examine the patient. That, in effect, is what we in American medicine, with the aid of others vitally interested in the health field, have been doing and are doing now. We are trying to find out what the aged really need; what new improvements are succeeding in giving them better health care and how such procedures can be universally applied.

For those of the aged who are in need of custodial care, we seek more realistically priced services in facilities especially designed for them. Too often they are now being treated in hospitals which provide—and charge for—many costly services which the average chronically ill aged patient does not need. These unnecessary services contribute to higher than necessary hospital costs for all of us.

The improvement of custodial care, and the upgrading of nursing home standards have been an objective for many years of the American Medical Association, the American Hospital Association and the American Nursing Home Association. To help meet these needs, testimony was presented on May 20, 1958 before the Subcommittee on Housing of the Senate Committee on Banking and Currency in favor of an amendment to the Federal Housing Administration Act to provide for government insured loans for hospitals and nursing homes.

The American Medical Association also believes that health facilities for the aged could be improved and expanded through greater use of Hill-Burton funds for chronic disease units of general hospitals and nursing homes by abolishing the categories presently contained in that Act. Such an amendment would permit the states to utilize their grants as best suits their individual needs. We made this recommendation in testimony presented on May 6, 1958 to the Subcommittee on Health of the Interstate and Foreign Commerce Committee of the House of Representatives.

Our studies also reveal that many aged patients are remaining in hospitals because there is often nowhere else for them to go—because there is no other local means by which state aid will pay for their care, or because it is the only way they can take advantage of their health insurance. A great many others remain overlong in the hospital because there is no local home-care program that would enable them to be cared for at home, among their family and friends.

A review is currently being made of community efforts to make it possible for many of these people to return to homelike surroundings. By providing the opportunity for the disabled elderly person to maintain a household, such local programs have not only produced the practical result of alleviating a local shortage of hospital beds and reducing the financial burdens on the individual, but they have also restored many patients to a useful life.

We are also attacking the problem of our mentally ill who are over 65. It is here that we confront the basic evil of senility. A number of experiments have demonstrated an almost miraculous recovery from mental stagnation when elderly patients were placed in more familiar surroundings and given new interests and social contacts. Recent isolated studies reveal that as high as 60% of the patients admitted to state mental hospitals did not require psychiatric treatment.

We are attempting to assist in devising a better means of meeting the health care costs for those of the aged who have no income, assets, or other means of support. Often unrealistic state indigent care programs aggravate the problem. States that have not allotted enough money for public assistance medical care are being urged to do so. At present, in excess of 300 million dollars is being spent by federal, state and local governments to provide medical care for public assistance recipients. The aged comprise more nearly ½ of the 5.6 million persons now receiving these public assistance benefits.

We believe that real progress is being made in bringing better health care to the aged and to all others who are ill, and in devising ways to lessen the economic burdens of prolonged illness. The number of persons receiving public assistance is declining. Health insurance coverage is increasing. Persons leaving industry and moving into retirement are bringing with them more and more retirement plans with progressively higher average benefits. Ultimate success in this effort will, however, finally depend upon local interest and action. Individual and community assistance has in the past helped to translate new medical knowledge into better health and greater life expectancy. These same forces which have been effective in the past will best help in solving the problem before us now.

In addition to the numerous and varied medical, scientific and socioeconomic activities being pursued in this field, the physicians of America for some time have recognized the need for additional organizational weapons to attack these problems. For many years the American Medical Association was an active participant in the affairs of the Commission on Chronic Illness. For the past several years the Association has had a Committee on Aging, composed of some of the leading medical authorities in the United States in this field, which has devoted its full effort to this problem. In addition, there are thirty-two Committees on Aging actively at work in the state medical societies. During the past year, the Association has conducted five regional conferences on aging in Seattle, Dallas, Philadelphia, Birmingham and Omaha. A national conference on aging will be sponsored by the American Medical Association in Chicago in September.

The American Hospital Association, likewise, has been conducting research and studying hospital practices with the objective of containing the rising costs of caring for the aged. Blue Shield and Blue Cross plans, as well as the health insurance companies, have stepped up their important contribution to the financing of medical care. They are now engaged in intensive studies designed to create new types of coverage tailored to meet the needs of the aged ill. Pre-retirement financing of health insurance policies with paid-up status at 65; use of life insurance after 65 to pay for health care; the application of deductible and co-insurance to permit coverage of costly illnesses at a low premium rate; and many other approaches are helping to spread health insurance coverage, to an ever increasing degree, among the aged. The nursing home operators are earnestly seeking to improve their standards and to provide a quality service that will bridge the present gap between inexpensive but inadequate home-care and adequate but overexpensive hospital care. Innumerable other instances could be cited of enterprising activity to analyze and meet the problem.

In addition to the independent activities of the American Medical Association and other groups and organizations, there has been a general realization of the need for a combined effort with the help of every independent person, association and agency that has something to contribute. With this in mind and in an effort to provide better coordination and stronger and swifter action in this area, the Joint Council to Improve the Health Care of the Aged has been formed. Some of the most important and respected organizations in the health field are the charter members. They are: the American Medical Association, the American Hospital Association, the American Dental Association and the American Nursing Home Association.

The Joint Council will explore the entire spectrum of problems relating to the aged and aging process. In broad outline the program of the Council will include a coordinated plan of research designed to:

(a) Determine the extent, utilization and availability of facilities, and the economic status and resources of the aged.

(b) Spearhead the expansion and experimentation in all types of voluntary health insurance coverage for the aged.

(c) Encourage the expansion of health care facilities for the aged.

(d) Encourage the development of community health services for the aged.

(e) Urge state and local legislative bodies to provide realistic financial support for medical, hospital and nursing home care of aged public assistance recipients, and

(f) Appraise the problems of the aged who are mentally ill and provide an intensification of education, research and action programs directed toward health problems of the aged at national, state and local levels.

In brief, the Joint Council and its member groups have adopted a positive, optimistic approach in an effort to apply their collective knowledge and skills in the improvement of the health care of the aged, to offer the aged a hope for a better existence and an opportunity to return to the mainstream of community life.

Gentlemen, this concludes my formal statement. It is our sincere recommendation that H. R. 9467, 85th Congress and similar bills not be favorably considered by this Committee.

June 28, 1958

Honorable Wilbur D. Mills
Chairman, Committee on Ways and Means
United States House of Representatives
Washington 25, D. C.

Dear Congressman Mills:

Our testimony presented yesterday was confined to a recital of the position of the American Medical Association concerning H. R. 9467, 85th Congress and similar bills. With your permission we would like to submit this supplementary statement concerning certain of the other measures under consideration by your Committee dealing with the Social Security program.

H. R. 8883, H. R. 9203 and H. R. 9835, 85th Congress would extend Title II of the Social Security Act so as to bring physicians, on a compulsory basis, under the Old Age, Survivors and Disability Insurance program. In as much as the House of Delegates of the American Medical Association has since 1949 consistently opposed such compulsory coverage for physicians, we would again like to register our opposition to these bills. We are not opposed to the voluntary inclusion of physicians under Title II such as proposed by H. R. 4824, 85th Congress.

In order to make individual retirement planning more feasible, our Association has advocated the passage of the Jenkins-Keogh bills, H. R. 9 and H. R. 10, 85th Congress. These bills would allow self-employed persons an adequate and preferable method of providing for their later years.

There are several bills now pending before your Committee which would amend the public assistance provisions of the Social Security Act with respect to the provision of medical care. The American Medical Association opposed the public assistance amendments of 1956 which set up a separate category for medical payments. In a letter to this Committee dated April 24, 1956, we stated that we saw no need for the establishment of a separate public assistance category for the provision of medical care, since the program then in effect was accomplishing, more flexibly, all that the 1956 amendments sought; that this new program would burden the local communities with regulations and restrictions inconsistent with their local problems and customs; and that the establishment of medical payments as a separate category under public assistance would be the forerunner to the establishment of medical care as a categorical benefit under the Old Age, Survivors and Disability Insurance provision of the Social Security Act.

The basic policy of our Association in regard to medical payments under public assistance was adopted by our House of Delegates in December, 1956. It is the belief of the Association that methods and amounts of payments for personal health services should be equitable and determined in the light of local conditions after consultation between the responsible public agency and representatives of the providers of such medical care.

That is to say, the individual states, with the advice of the state medical, hospital, and other professional organizations, should determine how much should be spent on medical services under the public assistance program and how these payments for medical service should be made. We are opposed, therefore, to any of the pending bills which would continue to deprive the states and the local health providers of their traditional right to determine the amount and method of medical care payments under public assistance programs.

There are other bills pending before your Committee which would expand and liberalize the disability benefit provisions written into Title II of the Social Security Act in 1956. Some of these bills would lower the present age limit of 50 or would do away with a minimum age limit altogether. Some would grant disability payments to dependents of disabled recipients or to their survivors. Some would lessen current coverage requirements for a person to receive disability payments and still others would liberalize the work-test on which the payments are predicated.

The American Medical Association vigorously opposed the enactment of these disability provisions in the 84th Congress. I refer you to our testimony before the Senate Finance Committee on February 23, 1956. We felt that this program was objectionable for medical reasons and that it would discourage many individuals from successfully rehabilitating themselves. We stated that permanent and total disability was impossible to determine in many cases and that this legislation would put tremendous pressure on physicians and the administering agency. Most importantly, we felt that once the payment of disability benefits was made a statutory right under the Social Security Act, it would be impossible to resist the pressures to expand the nature of the benefits and increase the number of beneficiaries.

A review of the administration of the disability program to date and an analysis of the pending bills indicate that our fears were justified. Just as we opposed the original enactment of the disability benefit program, we now oppose any bills which would liberalize it and further extend this medical-type payment program.

Finally, we would like to comment on H. R. 8883, 85th Congress. In addition to several other proposals, this bill would provide rehabilitation services for disabled workers to be paid for out of the Old Age, Survivors and Disability Insurance Trust Fund. The rehabilitation agencies would be required to enter a contract with the services to be provided determined by the Secretary of Health, Education and Welfare. Under the bill we would have state and private rehabilitation services being supervised by a Federal Government official and being paid for by the Social Security Trust Fund. We oppose this provision of rehabilitation services for the same basic reasons that we oppose the provision of hospital and surgical care under H. R. 9467, 85th Congress.

We wish to thank you and the members of the Committee on Ways and Means for allowing us to present our views on these matters both at the recent hearings and in this letter. If any members of the Committee desire further information concerning our positions on the subjects covered, we would be only too happy to furnish anything we have.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

WISCONSIN CONGRESSIONAL DELEGATION HONORS DR. GUNDERSEN

Dr. Gunnar Gundersen, newly elected President of the American Medical Association, made his first public appearance after the A. M. A. annual convention as a guest of the Wisconsin members of the Senate and House of Representatives. At a breakfast in the Capitol, Dr. Gundersen was praised by members of both parties for the Gundersen family contribution to medicine and public service for over half a century. Representative Withrow said, in introducing the doctor, that three generations of Gundersen doctors had treated him and his family for over 50 years.

Attending the breakfast are seated, left to right, Congressman Byrnes, Dr. Kennard, Senator Wiley, Dr. Gundersen, Congressman Withrow, and Senator Proxmire; standing left to right, Congressmen Tewes and Van Pelt, Attorney Kuehl, Congressmen Johnson, Laird, Zablocki, O'Konski, and Reuss, and Drs. Maxwell and Davis.

Senator Wiley and Representative James Byrnes, leader of the Republican delegation in the House, arranged the affair. It marked the first time the entire Wisconsin delegation had gathered together. Senator Proxmire said he had been greatly impressed by the strength of the A. M. A. in regard to federal legislation.

Dr. Gundersen observed that more good will could be attained in the international field if the United States were to use funds for foreign aid to provide aid to alleviate medical problems abroad.

Others attending the breakfast were Representatives Donald E. Tewes, William K. Van Pelt, Lester R. Johnson, Melvin R. Laird, Clement J. Zablocki, Alvin E. O'Konski, Gardner R. Withrow, and Henry S. Reuss, and Drs. William Kennard, Cyrus Maxwell, and Joseph Davis, and Frank Kuehl of the Washington Office of the A. M. A.

Postgraduate Courses for Physicians

Compiled by the Council on Medical Education and Hospitals for the Period Sept. 1, 1958 to Aug. 31, 1959

The data in the following list of postgraduate courses have been compiled by the staff under the supervision of Dr. Glen R. Shepherd, Assistant Secretary of the Council on Medical Education and Hospitals, with the clerical assistance of Miss Eileen O'Brien. The Council desires to express appreciation to the officers of the medical schools, hospitals, and medical societies who have cooperated in furnishing the information essential to the preparation of this report.

Edward L. Turner, M.D., Secretary
Council on Medical Education and Hospitals

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INTRODUCTION

The fourth annual listing of postgraduate courses in this country for physicians appears in the following pages of The Journal. This listing is for the period Sept. 1, 1958, to Aug. 31, 1959. The annual list replaces the semiannual lists that appeared previously.

Postgraduate medical education courses consist of planned activities for doctors of medicine intended to refresh practicing physicians in the various aspects of their basic medical education, to provide information on new developments in medicine, and to stimulate further educational efforts by the participants. Such courses are not designed to provide the lengthy intensive education required for specialist training, and thus they usually do not lead either to credit toward graduate degrees or to specialty board certification. These are in the field of graduate medical education and usually consist of residency training or fellowships. Postgraduate courses are shorter than graduate education programs.

This list of postgraduate courses was prepared from the unappraised and unevaluated replies to Council questionnaires by American medical schools, hospitals, and the various national, state, and specialty medical societies. This list is printed simply to provide for those physicians seeking postgraduate courses a point of departure through which further information can be obtained by writing to the institution or organization listed under Location. Inquiries should be made before traveling to any course listed, because dates, time arrangements, and fees are subject to change. Sponsors of courses having numerical limitation of registration must restrict enrollment, often on the basis of order of application. Courses for which there is insufficient advance registration may be canceled. Such inquiry of the sponsor is especially urged about courses scheduled for 1959, on which final information may not have been available to the sponsor at the time this list was prepared.

Though the educational values of medical society meetings and conventions as well as hospital staff and departmental meetings can be very real and worthwhile, such meetings are not usually listed here as postgraduate courses. Lists of meetings are to be found periodically elsewhere in The Journal.

Many of the courses have co-sponsors to whom specific credit cannot be given because of space limitations. It is expected that the institution or organization sponsoring the course has provided such co-sponsor recognition to its registrants.

Under each category in the following list, the order of arrangement of the courses is alphabetically first by states, second by cities within states, third by the institutions and organizations within the cities, and last by date of course where several courses in that category are offered by the same institution or organization.

Although the list may indicate that a course is designed primarily for specialists in that category, many such courses are open to any physician, so specific inquiry should be made of the institution listed.

One of the categories has a special use in addition to its usual denotation. In the General Practice category are listed those courses having subjects embracing several fields, such as a course on the management of mass casualties or the Summer School of Alcohol Studies.

The Council on Medical Education and Hospitals has studied continuing medical education for several years. Following the 1952-1955 survey, its ad hoc Advisory Committee on Postgraduate Medical Education was appointed and met first in June, 1956. The Committee has considered ways in which the Council can be of greatest assistance in the further development of this part of medical education. As an initial step in such a course of action recommended by the Advisory Committee and endorsed by the Council, the House of Delegates of the American Medical Association adopted in June, 1957, a document entitled "A Guide Regarding Objectives and Basic Principles of Postgraduate Medical Education Programs." This guide should be of interest to all who are active in sponsoring such programs. Copies may be obtained on request to the Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

KEY

Designed For

G—General practitioners
S—Specialists
B—Both
Lim—Enrollment limited to specified number with number stated; i. e., Lim 20, meaning enrollment limited to 20 in the course. If it is repeated, another 20 could be accommodated

Type

IC—Intensive continuous
II—Intensive intermittent
CC—Circuit course
PT—Postgraduate traineeship*
HS—Home study
HS (C)—Home study by correspondence
HS (R)—Home study by radio
O—Other

Time Arrangement

C—Continuous or concentrated (e. g., as every day for five days)
I—Intermittent (e. g., every Thursday for six weeks)

Methods of Education

AV—Audiovisual aids (movies, slides, models)
BR—Bedside rounds
Clin C—Clinical conference
Dem—Demonstrations other than of patients
EPP—Enrolee performs procedure
LC—Live clinic
Lab—Laboratory work (including cadaver dissection and dog surgery where applicable)
Lec—Lecture
O—Open question periods
PD—Patient demonstration
Pan—Panel discussion
PT—Postgraduate traineeship*
R—Radio or telephone
Sem—Seminar
Surg—Operative human surgery
TV—Television

*A postgraduate traineeship for practicing physicians is an individually arranged residency-type postgraduate educational experience in a hospital usually with residents in that field. It differs from a residency or fellowship in the following ways: 1. It is not primarily intended to provide training for entering specialty practice or, in itself, to qualify for specialty board certification. 2. Therefore, it is of shorter duration than a year. 3. It usually does not provide either a stipend or housing, and it may exact a fee from the physicians in such training. 4. It may not (or may) involve direct patient responsibility.

ALLERGY

(See also Pediatrics)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Allergies	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, AV	6	Spring/59	Same day	C; 1 day	20
The American Academy of Allergy Postgraduate Course	The American Academy of Allergy 756 N. Milwaukee St., Milwaukee; course at a Chicago hotel	S	IC	Lec, Pan, O, AV	14	2/ 7/59	2/ 8/59	C; 2 days	25
Asthma, Hay Fever and Allied Diseases	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	500	Arranged by appointment	6 mo. later	6 mo. full time	500
Personal Course in Allergy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	500	Arranged by appointment	6 mo. later	6 mo. full time	500
Asthma, Hay Fever and Allied Diseases	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	140	1st Monday each mo. Monthly	Saturday of 4th wk.	24 days	200
Personal Course in Allergy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Lec, O, EPP	140	1st Monday each mo. Monthly by appointment	Saturday of 4th wk.	24 days	200
Allergy for General Physicians and Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	B	IC	Lec, O, AV	15	4/ 6/59	4/ 8/59	C; 3 days	40
Allergy	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	21	3/25/59	3/27/59	C; 3 days	45
Medicine PM 68-Allergy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	LC, Lec, O, AV	26	9/11/58	12/18/58	I; 13 sessions 2 hr. weekly, Thursdays	50
Allergy	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	II	Lab, PD, LC, Clin C, Lec, O	16	Arranged		I; 8 sessions 2 hr. weekly, Thursdays	50
5415-A. Allergy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	105	12/ 1/58	12/19/58	C; 15 days	250
5417-A. Refresher Course in Allergic Conditions	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	21	3/23/59	3/25/59	C; 3 days	55
5432-A. Allergy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	16	4/10/59	5/29/59	I; 8 sessions 2 hr. weekly, Fridays	
Allergy in Theory and Practice	Roosevelt Hospital Institute of Allergy 428 W. 59th St., New York 19	B Lim 40	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O	40	5/11/59	5/16/59	C; 5 days	100
General Allergy	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 20	II	PD, LC, Sem, Lec	36	10/23/58	1/29/59	I; 12 sessions 3 hrs. weekly, Thursdays	60
Clinical Allergy	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 10	II	Lec, Pan, AV	Unknown	1/59	5/59	Unknown	25
Clinical Allergy	Montefiore Hospital 5th Ave., Pittsburgh	G Lim 50	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	30	4/ 6/59	4/11/59	C; 5 days	60
Allergy—Part I	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex	S	IC	Lab, Lec, O, AV	16	2/59	2/59	C; 3 days	35

ANATOMY

(See also Gynecology, Ophthalmology, Otolaryngology)

Surgical Anatomy—Dissection, Lectures and Demonstrations	College of Medical Evangelists 1720 Brooklyn Ave, Los Angeles 33	G Lim 30	II	Lab, Sem, Lec, Dem	318	9/ 8/58	6/ 4/59	I; 71 sessions 4½ hr twice weekly, Mondays, Wednesdays	250
Surgical Anatomy—Lectures and Demonstrations	College of Medical Evangelists 1720 Brooklyn Ave, Los Angeles 33	G Lim 15	II	Lec, Pan, Dem	82	9/10/58	6/ 3/59	I; 41 sessions 2 hr weekly, Wednesdays	100
Surgical Anatomy	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 30	II	Lab, Lec, O, AV, EPP	20	Fall/58		I; 10 sessions 2 hr.	Unknown
Gross and Applied Anatomy	San Diego County General Hospital North end of Front St, San Diego 3, Calif	S Lim 20	II	Lab, Lec, O, AV	32	9/58	12/58	I; 16 sessions 2 hr weekly, Wednesdays	Nil
Neuroanatomy	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology, Connecticut State Hospital, Middletown, Conn; course at Yale University School of Medicine, New Haven, Conn	S Lim 40	II	Lec, O	9	9/21/58	11/16/58	I, 9 sessions 1 hr weekly, Wednesdays	Nil
Anatomy 201—Special Dissections in Anatomy	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St, New Haven, Conn	S Surgery and Surgical Specialties	II	Lab, EPP	Arranged	Arranged			Arranged
Anatomy 202—Demonstration in Anatomy	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St, New Haven, Conn	S Surgery and Surgical Specialties	II	Lab, O, AV	50	9/58	5/59	I; 50 sessions 1½ to 2 hr weekly, day to be arranged	175
Surgical Anatomy	University of Colorado School of Medicine 4200 E Ninth Ave, Denver 20	B Lim	IO	Lab, Lec	180	3/59	6/59	C; 3 hr daily	Unknown
Dissection of Female Abdomino Pelvis	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV, EPP	60	Arranged	4 mo after beginning	I; 15 sessions 4 hr weekly, Tuesdays	125
Anatomy for Anesthesiologists	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV	Arranged	9/58	6/59	I; once weekly, hr and days not determined	50
Surgical Anatomy on the Cadaver and Clinical Surgery	Cook County Graduate School of Medicine 707 S Wood St, Chicago 12	G Lim 20	IO	Lab, PD, LO, BR, Clin C, Surg, Lec, O, AV	100	3/ 2/59	3/14/59	C; 13 days	150
Dissection of Lower Extremity for Orthopedic Surgeons	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV, EPP	56	Arranged	14 wk after beginning	I; 14 sessions 4 hr weekly, Thursdays	75
Dissection of Spine for Orthopedic Surgeons	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV	56	Arranged	14 wk after beginning	I; 14 sessions 4 hr weekly, Thursdays	75
Dissection of Upper Extremity for Orthopedic Surgeons	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV, EPP	56	Arranged	14 wk after beginning	I; 14 sessions 4 hr weekly, Thursdays	75
Embryology for Otolaryngologists	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV	16	Arranged Fall	4 wk after beginning	I; 4 sessions 4 hr. weekly, Mondays	25
Dissection of Male Abdomino Pelvis	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 5	II	Lab, Lec, O, AV	32	4/27/59	6/15/59	I; 8 sessions 4 hr. weekly, Mondays	125
General Anatomy	University of Maryland School of Medicine Lombard and Greene Sts, Baltimore	S Lim 3	IO or II	Lab, Lec, Pan	Arranged	Arranged	Arranged		Unknown
Anatomy of Head and Neck as Applied to the Ear, Nose and Throat	University of Maryland School of Medicine Lombard and Greene Sts, Baltimore	S Lim 6	II	Lab, Sem, AV, EPP	20	10/58	4/59	I; 10 sessions 2 hr weekly, Thursdays	25
Clinical Anatomy	University of Maryland School of Medicine 522 W. Lombard St, Baltimore	S Lim 20	II	Lab, Lec	90	1/20/59	5/15/59	I; 30 sessions 3 hr. twice weekly, Mondays, Wednesdays	150
Surgical Anatomy	Harvard Medical School, Courses for Graduates 25 Shattuck St, Boston 15	S Lim 16	IO	Lab, Lec	140	3/ 2/59	4/24/59	C; 40 days	200
Surgical Anatomy of the Head and Neck	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St, Newark, N. J.; course at Martland Medical Center, Newark, N J	S Lim 25	II	Lab, Lec, O	7½	10/ 3/58	11/ 7/58	I; 5 sessions 1½ hr. weekly, Fridays	75

Key will be found on page 1954.

ANATOMY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Surgical Anatomy of the Chest	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 20	II	Lab, Lec, O	7½	10/10/58	11/ 7/58	I; 5 sessions 1½ hr. weekly, Fridays	75
Surgical Anatomy of Pelvic and GU Tract	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 20	II	Lab, Lec	9	10/19/58	12/19/58	I; 6 sessions 1½ hr. weekly, Fridays	100
Surgical Anatomy of the Extremities and Vertebrae for Orthopedic Surgeons	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 20	II	Lab, Lec, O, EPP	12	1/ 9/59	2/27/59	I; 8 sessions 1½ hr. weekly, Fridays	125
Surgical Anatomy—Dissection of Upper Extremity	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, EPP	21½	9/16/58	10/28/58	I; 7 sessions 3½ hr. weekly, Tuesdays	100
Surgical Anatomy—Dissection of Head and Neck	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, EPP	31½	11/ 4/58	1/13/59	I; 9 sessions 3½ hr. weekly, Tuesdays	150
Surgical Anatomy—Dissection of the Thorax	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, EPP	17½	1/20/59	2/17/59	I; 5 sessions 3½ hr. weekly, Tuesdays	75
Surgical Anatomy—Dissection of Abdomen	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, EPP	24½	2/24/59	4/ 7/59	I; 7 sessions 3½ hr. weekly, Tuesdays	100
Surgical Anatomy—Dissection of Lower Extremity	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 20	II	Lab, Sem, EPP	17½	4/15/59	5/12/59	I; 5 sessions 3½ hr. weekly, Tuesdays	75
Surgical Anatomy—Review	Cornell University Medical College 1300 York Ave., New York	S Lim 25	IC	Lab, Lec, O, AV, EPP	180	5/25/59	6/20/59	C; 24 days	200
Anatomy—Surgical (a) (Cadaver demonstration)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 6	II	Lec, O, AV, EPP	18	Arranged		I; 6 sessions 3 hr. thrice weekly, Mondays, Wednesdays, Fridays	300
Anatomy—Surgical (b) (Cadaver demonstration)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	II	Lec, Pan, O, AV, EPP	18	Arranged		I; 6 sessions 3 hr. thrice weekly, Mondays, Wednesdays, Fridays	300
Anatomy—Surgical (c) (Cadaver demonstration)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	II	Lec, O, AV, EPP	12	Arranged		I; 6 sessions 2 hr. thrice weekly, Mondays, Wednesdays, Fridays	Unknown
Anatomy—Surgical (d) (Cadaver demonstration)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	II	Clin O, Lec, O, AV, EPP	6	Arranged		Unknown	300
396-A. Anatomy of the Head, Neck and Thorax for Otolaryngologists	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 8	IC	Lab, Lec, O, EPP	90	9/15/58	10/24/58	C; 30 days	150
113-A. Surgical Anatomy of the Abdomen	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/22/58	12/12/58	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
111-A. Surgical Anatomy of the Head and Neck	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/22/58	12/12/58	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
112-A. Surgical Anatomy of the Thorax and its Viscera	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	144	9/22/58	12/12/58	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
553-A. Anatomy for Orthopedic Surgeons	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	Lab, O, EPP	35	1/12/59	1/16/59	C; 5 days	150

414-A. Surgical Anatomy of the Female Pelvis	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	141	3/23/59	6/12/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
415-A. Surgical Anatomy of the Genitourinary System	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	141	3/23/59	6/12/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
416-A. Surgical Anatomy of the Musculoskeletal System	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	II	Lab, Sem, Lec, AV, EPP	141	3/23/59	6/12/59	I; 36 sessions 4 hr. thrice weekly, Mondays, Wednesdays, Fridays	100
Anatomy	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	B	IC or II	Lab, EPP	Arranged	Arranged	Arranged		Arranged

ANESTHESIOLOGY

(See also Anatomy, Cardiovascular Disease)

Anesthesiology in General Practice	Lloyd Noland Hospital and Clinic P. O. Box 538, Fairfield, Ala.	G Lim 8	IC or II	PD, LC, BR, Clin C, Surg, Lec, Pan, O, AV, EPP	Full time with night call, or 6 hrs. daily	Arranged		Arranged	Varies
Anesthesiology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33; course at White Memorial Hospital, Los Angeles 33	G Lim 2	IC	LC, Sem, Lec	765	Unknown Every 6 mo.	6 mo. after starting date	C; 120 days	350
Current Concepts in Anesthesia	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	19	8/27/59	8/29/59	C; 3 days	50
Anesthesiology	University of Colorado School of Medicine 1200 E. Ninth Ave., Denver 20	G Lim	PT	LC, Clin C, Sem, Surg, EPP	Varies	Arranged		Arranged	Unknown
Course I—Regional Anesthesia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 1	IC	Lab, PD, LC, Sem, Surg, Lec, O, EPP	140	1st Monday each mo. Monthly by appointment	Friday of 4th wk.	C; 20 days	300
Course V—Inhalation and Endotracheal Anesthesia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 5	IC	Lab, PD, LC, Sem, Surg, Lec, O, EPP	140	1st Monday of each mo. By appointment monthly	Friday of 4th wk.	C; 20 days	300
General Anesthesiology Traineeship	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	PT	Lab, PD, LC, BR, Sem, Lec, Pan, O, AV, EPP	80, 160 or 320	Each Monday	Varies	11, 28, or 56 days	100, 150, or 200
Anesthesiology for the General Practitioner and the Part-time Anesthesiologist	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Clin C, Lec, Pan, O, AV	14	2/18/59	2/19/59	C; 2 days	25
Postgraduate Traineeship	State University of Iowa Hospitals Iowa City	G Lim 2	PT	PD, Clin C, Sem, O, EPP		Arranged		Arranged	Nil
Anesthesia for the Part-time Anesthetist	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IC	PD, Lec, Pan, O, AV	6	10/ 9/58	10/ 9/58	C; 1 day	15
Clinical Traineeship in Anesthesiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G Lim 1	PT	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	Varies	Arranged		11 to 30 days	50 per mo. in state; 100 per mo. out of state
Anesthesiology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	PD, Clin C, Lec, Pan, O, AV	21	4/13/59	4/15/59	C; 3 days	40
Anesthesia	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IC	Clin C, Sem, Lec, Pan	20	3/ 5/59	3/ 7/59	C; 2½ days	25
Anesthesiology	Eastern Maine General Hospital Bangor, Me.	G Lim 2	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV, EPP	Varies	Arranged		Arranged	Nil
Anesthesiology	Central Maine General Hospital 300 Main St., Lewiston, Me.	G Lim	PT	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	Varies	Arranged		Arranged	Nil
Postgraduate Lectures in Anesthesiology	Maine Medical Center 22 Bramhall St., Portland, Me.	G	II	Sem, Lec, O, AV	15	10/17/58	5/59	I; 15 sessions 1 hr. each	Nil
Post Graduate Training in Anesthesiology	St. Vincent Hospital 25 Winthrop St., Worcester, Mass.	G Lim 2	PT	PD, BR, Clin C, Lec, Pan, O, EPP	Varies	Arranged		3 to 6 mo.	Nil
Clinical Anesthesiology	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G Lim 6	PT	PD, LC, BR, Clin C, Sem, Lec, EPP	320	1/ 1/59 4/ 1/59 7/ 1/59	3/31/59	90 days	200

Key will be found on page 1954.

BASIC SCIENCES—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Physiology PM 33-Gastrointestinal	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Sem, O, AV	60	10/58	5/59	I; 1 hr. twice weekly	100
Physiology PM 32-Normal and Pathological Physiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lec, O, AV	52	10/ 1/58	4/59	I; 26 sessions 2 hr. weekly, Wednesdays	150
Physiology PM 30-Digestive Tract	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lec, O, AV	36	1/ 7/59	5/ 6/59	I; 18 sessions 2 hr. weekly, Wednesdays	100
555-A. Electronics for Physicians	New York University Post-Graduate Medical School 550 First Ave, New York 16	G Lim 30	II	Lec, O, AV	15	9/ 2/58	11/11/58	I; 10 sessions 1½ hr. weekly, Tuesdays	75
544-A. Normal and Pathological Physiology: Functional and Chemical Aspects	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	70	9/15/58	9/26/58	C; 10 days	125
460-A. Biochemistry and Physiology in Disease: Laboratory Diagnosis	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	II	PD, Clin C, Lec, O	16	9/30/58	11/25/58	I; 8 sessions 2 hr. weekly, Tuesdays	50
644-A. Neuroanatomy and Neurophysiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	II	Lab, Lec	126	9/15/58	12/ 5/58	I; 36 sessions 3½ hr. thrice weekly, Mondays, Wednesdays, Fridays	350
461-A. Clinical Physiology: The Application of Basic Physiology to Diagnostic and Therapeutic Problems	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 35	II	Clin C, Sem, Lec, O, AV	16	1/ 8/59	2/26/59	I; 8 sessions 2 hr. weekly, Thursdays	50
5426-A. Normal and Pathological Physiology: Functional and Chemical Aspects	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	16	4/ 8/59	5/27/59	I; 8 sessions 2 hr. weekly, Wednesdays	60
Heterologous Transplantation of Human Tumors and other Tissues	Sloan-Kettering Institute 410 E. 68th St., New York	S Lim 25	IC	Lab, Sem, Lec, Pan, O, EPP	24	10/ 7/58 3/10/59	10/ 9/58	C; 3 days	Nil
Correlated Clinical Science Course	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G	IC	Lec, O, AV	160	9/23/58	1/24/59	C; 4 mo.	250

CARDIOVASCULAR DISEASE

(See also Anesthesiology, Electrocardiography, Internal Medicine, Pediatrics, Peripheral Vascular Disease, Radiology, Surgery)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Cardiovascular Symposium	Fresno County Heart Association 329 N. Van Ness, Fresno, Cal.; course at Hotel Californian or Motel Hacienda, Fresno, Calif.	G	IC	Sem, Lec, Pan, O, AV	8	1/59	1/59	C; 1 day	12.50
Cardiac Resuscitation	Los Angeles County Heart Association 660 S. Western Ave., Los Angeles 5; course at University of Southern California School of Medicine, Los Angeles 33	G Lim 8	IC	LC, EPP	2	9/3/58 each Wednesday	9/3/58	C; 1 day	30
Pathological Physiology of the Cardiovascular System	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 25	II	Sem, Lec, Pan, O, AV	20	Fall/58		I; 10 sessions 2 hr. weekly, Mondays	60
Selected Topics in the Pathological Physiology of the Cardiovascular System	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 25	II	Sem, Lec, Pan, O, AV	20	10/6/58	12/8/58	I; 10 sessions 2 hr. weekly, Mondays	60
873—Cardiac Resuscitation	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	B Lim 5	II	Lab, Lec, EPP	2	continuous weekly		I; 1 session 2 hr. weekly, Wednesdays	30 practicing physicians; Nil residents, interns, Armed Forces
852—Cardiac Diagnosis	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G Lim 10	II	PD, LC, BR	24	Spring/59		I; 12 sessions 2 hr. weekly, Wednesdays	65

Symposium of Cardiovascular Disease	University of California Medical Extension San Francisco course at Odd Fellows Hall Santa Rosa, Calif	G Lim 8	IC	Lec	9	11/12/58	11/12/58	C, 1 day	12 50
Third Annual Post Graduate Symposium on Heart Disease	Santa Clara and San Mateo County Heart Associations 181 2nd Ave, San Mateo, Calif	G	IC	Sem, Lec, Pan, O, AV	6	Unknown		C, 1 day	5
Symposium on Heart Disease	Orange County Heart Association P O Box 1704, Santa Ana, Calif	G	IC	Lec, Pan, O, AV	8 10	Spring/59		C, 1 day	12 50
Annual Symposium on Heart Disease	Santa Barbara County Heart Association 18 La Arcada Court Santa Barbara, Calif, course at Biltmore Hotel, Santa Barbara, Calif	B Lim 100	IC	Sem, Lec, Pan, O, AV	8	11/ 1/58	11/ 1/58	C; 1 day	20
Cardiac Physiology in Relation to Cardiac Disease	University of Colorado School of Medicine 4200 E Ninth Ave, Denver 20	B	II	Sem, Lec		4/59	6/59	I, once weekly for 12 wk	10
8th Annual Western Cardiac Conference	Office of Postgraduate Medical Education University of Colorado School of Medicine 4200 E Ninth Ave, Denver 20	B	IC	PD, Lec, Pan, O, AV	40	8/59	8/59	C, 5 days	20
Seminar on Cardiovascular Diseases	Northeast Florida Heart Association 425 W Duval St, Jacksonville, Fla	B	IC	Clin C, Sem, Lec, Pan O, AV	15	2/59		C, 2½ days	10
Cardiac Resuscitation	Postgraduate Education Emory University School of Medicine 69 Butler St, S E, Atlanta, Ga	G	IC	PD Sem, Lec, Pan, O, AV	10	10/ 3/58	10/ 3/58	C, 1 day	20
Treatment of Heart Disease	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	G	IC	Lec, Pan, O, AV	7	4/20/59	4/20/59	C, 1 day	10
Cardiac Auscultation	State University of Iowa College of Medicine University Hospitals, Iowa City	S Lim 30	IC	PD, Lec, Pan, O, AV	12	4/ 8/59	4/ 9/59	C, 2 days	15
Cardiac Auscultation	University of Kansas Medical Center 39th and Rainbow Blvd, Kansas City, Ks	G Lim 20	IC	PD Lec, O, AV, LPP	14	10/13/58 3/23/59	10/14/58	C, 2 days	50
Clinical Traineeship in Cardiovascular Disease	University of Kansas Medical Center 39th and Rainbow Blvd, Kansas City, Ks	G Lim 2	PI	Lab, PD, LC, BR Clin C, Sem, Lec, O, AV, LPP	120	2/ 2/59 3/ 2/59	2/28/59	Approximately 30 days	200
Annual Scientific Sessions On Heart Disease	Heart Association of Maryland 1140 Mondawmin Concourse, Baltimore 15 course at University of Maryland Hospital Baltimore	S	IC	Lec Pan O, AV	7	9/58	9/58	C, 1 day	Unknown
First Postgraduate Course in Cardiology—Surgery and Current Concepts	Heart Association of Maryland 1140 Mondawmin Concourse Baltimore 15, course at Johns Hopkins Hospital, Baltimore	G	IC	PD LC, BR Clin C Sem, Lec, Pan, O, AV	20	1/15/59	1/17/59	C, 3 days	Unknown
Cardiovascular Disease	Harvard Medical School, Courses for Graduates 25 Shattuck St, Boston 15; course at Massachusetts General Hospital, Boston 14	S Lim 12	IC	Lab, PD LC, BR, Clin C, Lec, O	35 40 hr/wk	10/ 1/58	5/31/59	C, 8 mo	800
Cardiology 1	Harvard Medical School, Courses for Graduates 25 Shattuck St, Boston 15, course at Beth Israel Hospital, Boston 15	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, O	450	2/ 2/59	4/30/59	C, 60 days	500
Diseases of the Heart	University of Michigan Medical School, Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	35	4/ 6/59	4/10/59	C, 5 days	50
Cardiovascular Diseases for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	15	2/23/59	2/25/59	C; 3 days	40
Cardiovascular Seminar	University of Mississippi Medical Center, Secretary, Postgraduate Education Committee 2500 N State St, Jackson, Miss	B Lim 150	IC	PD, Sem, Lec, Pan, O, AV	20	4/ 1/59	4/ 3/59	C; 3 days	10
Cardiac Ausculation	St Louis University School of Medicine 1402 S Grand Blvd, St Louis 4, course at Firmin Desloge Hospital, St Louis 4	G Lim 35	IC	PD, Sem, Lec, Pan, O, AV, LPP		Arranged		Arranged	Unknown
Advanced Clinical Electrocardiography	St Michael's Hospital 306 High St, Newark, N J	G Lim 50	II	Lec	16	9/58	2/59	I, 10 sessions 1 hr biweekly, Wednesdays	Unknown
Recent Advances in Clinical Cardiology	St Michael's Hospital 306 High St, Newark, N J	G Lim 50	II	PD, LC, BR, Clin C, Lec, O, AV	16	9/58	2/59	I, 8 sessions 2 hr biweekly, Wednesdays	25
Applied Cardiology—Recent Advances	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St, Newark, N J; course at Elizabeth General Hospital, Elizabeth, N J	G Lim 45	II	Lec, O, AV	15	9/25/58	1/23/59	I, 10 sessions 1½ hr weekly, Thursdays	Unknown

Key will be found on page 1954.

CARDIOVASCULAR DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Cardiac Resuscitation Course	St. Michael's Hospital 306 High St., Newark, N. J.	S Lim 12	IC	Lab, Lec, O, AV, EPP	7	10/58 repeated one Saturday of each mo. for 8 mo.	5/59	C; 1 day	25
Modern Concepts in Cardiology	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Francis Hospital, Trenton, N. J.	G Lim 45	II	Lec, O, AV	15	Unknown		I; 10 sessions 1½ hr. weekly	50
Selected Cardiovascular Disorders	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	11/6/58	11/6/58	C; 1 day	12
Recent Advances in Cardiovascular Diseases	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	2/ 5/59	2/ 5/59	C; 1 day	12
Medicine PM 64-Surgical Treatment of Heart Diseases	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	Clin C, Sem, Lec, O, AV	66½	9/23/58 2/ 3/59	1/27/59	I; 19 sessions 3½ hr. weekly, Tuesdays	150
Medicine PM 60-Cardiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	Lab, Lec, O, AV	96	9/25/58 2/ 5/59	1/29/59	I; 16 sessions 6 hr. weekly, Thursdays	150
Medicine PM 62-Cardiology II	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, Lec, O, AV	56	9/25/58 2/ 5/59	1/29/59	I; 16 sessions 3½ hr. weekly, Thursdays	150
Medicine PM 63-Cardiology III	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 20	II	Sem, Lec, O, AV	56	9/25/58 2/ 5/59	1/29/59	I; 16 sessions 3½ hr. weekly, Thursdays	150
Medicine PM 29-Clinical Cardiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	PD, LC, Lec, O, AV	20	10/14/58 2/ 3/59	12/16/58	I; 10 sessions 2 hr. weekly, Tuesdays	60
Medicine PM 31-Recent Advances in Cardiovascular Disease	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IC	PD, Lec	30	1/26/59	2/ 6/59	C; 10 days	75
Medicine PM 48-Heart Disease and Circulatory Dynamics	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	PD, LC, BR, Lec, O, AV, EPP	20	2/17/59	4/21/59	I; 10 sessions 2 hr. weekly, Tuesdays	50
Clinical Cardiology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Beth-El Hospital, Brooklyn, N. Y.	G Lim 6	II	Lec, AV	18	4/ 8/59	5/21/59	I; 12 sessions 1½ hr. twice weekly, Wednesdays, Fridays	30
Cardiac Surgery—Recent Advances	New York State Heart Assembly 105 E. 22nd St., New York 10; course at Hotel Sheraton, Rochester, N. Y.	G	IC	Lec, Pan, O, AV	6	3/19/59	3/19/59	C; 1 day	Nil
546-A Modern Methods in the Recognition and Treatment of Heart Disease	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	II	PD, Clin C, Lec, O, AV	16	10/16/58	12/11/58	I; 8 sessions 2 hr. weekly, Thursdays	55
517-A. Diagnostic Cardiac Auscultation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	IC	Lab, PD, Lec, O, AV	21	10/22/58 2/26/59	10/24/58	C; 3 days	60
5416-A. Modern Trends in The Diagnosis and Treatment of Congenital Heart Disease	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, Lec, AV	21	2/ 4/59	2/ 6/59	C; 3 days	55
5418-A. Cardiac Roentgenology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	IC	Lab, PD, Lec, O, AV	14	4/ 3/59	4/ 4/59	C; 2 days	40
5430-A. Cardiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	II	PD, Lec, AV	24	4/ 9/59	5/28/59	I; 8 sessions 3 hr. weekly, Thursdays	85
64[illegible] A. Modern Concepts in the Diagnosis and Treatment of Heart Disease	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 60	IC	Lec, Pan, O	42	5/11/59	5/16/59	C; 6 days	100

Cardiovascular Diseases	*Rochester General Hospital* 601 W. Main St., Rochester, N. Y.	G	II	PD, Clin C, Lec, Pan, O, AV	10	9/11/58	11/6/58	I; 8 sessions 2 hr. weekly, Thursdays	20
Seminars on Heart Disease	*St. Francis Hospital and Sanatorium* Roslyn, N. Y.	G Lim 75	II	Sem, Lec, O	8	9/58	5/59	I; 4 sessions 2 hr. bi-monthly, Thursdays	Nil
Postgraduate Course in Cardiology	St. Francis Hospital and Sanatorium Roslyn, N. Y.	G Lim 60	IC	PD, Sem, Surg, Lec, Pan, O, AV, TV	82	4/18/59	4/25/59	C; 12 days	Unknown
Congenital Heart Disease	*American College of Physicians* 1200 Pine St., Philadelphia 4; course at The Johns Hopkins Hospital, Baltimore	S	IC	PD, Clin C, Lec, Pan, O, AV	35-40	11/17/58	11/21/58	C; 5 days	30 A.C.P. members; 60 Non-members
Recent Advances in Cardiovascular Disease	*American College of Physicians* 1200 Pine St., Philadelphia 4; course at Mount Sinai Hospital, New York	S	IC	Lec, Pan, O, AV	35-40	2/ 9/59	2/13/59	C; 5 days	30 A.C.P. members; 60 Non-members
1959 Cardiologic Sessions for Practicing Physicians	American Heart Association 44 E. 23 St., New York; course at Philadelphia Trade and Convention Center, Philadelphia	S	IC	Lec, Pan	7	10/23/58	10/23/58	C; 1 day	Nil for members
Postgraduate Cardiology Course No. 1	Hahnemann Medical College and Hospital 235 N. Broad St., Philadelphia	G Lim 50	II	PD, Lec, O, AV	90	10/58	5/59	I; 30 sessions 3 hr. weekly, Thursdays	150
Postgraduate Cardiology Course No. 2—Electrocardiography, *X-Ray, Auscultation*	Hahnemann Medical College and Hospital 235 N. Broad St., Philadelphia	G Lim 20	II	PD, Clin C, Lec, O, AV	45	10/58	5/59	I; 30 sessions 1½ hr. weekly, Thursdays	150
Cardiac Arrhythmias	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 40	IC	Unknown	Unknown	Fall/58	Unknown	Continuous	75
The Newer Advances in the Hypertensive Management of the Cardiac Patient	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at City Health Auditorium—City Health Building, Austin, Tex.	G Lim 150	IC	Lec, Pan, AV	15	9/16/58	9/17/58	C; 2 days	30
Cardiology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at Turner Home, El Paso, Tex.	G	IC	Lec, O, AV	7	10/11/58	10/11/58	C; 1 day	10

CLINICAL PATHOLOGY

(See also Ophthalmology)

Refresher Course for Laboratory Medical Officers	Department of the Army *Office of the Surgeon General* Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D.C.	S Restricted to military personnel Lim 20	IC	Lab, Sem, Lec, Pan, O, AV, EPP	45	2/ 9/59	2/14/59	C; 6 days	Nil
teriophage Typing of Staphy- occi (8.56)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's doing epidem. and research on Staph. Lim 2	IC	Lab, EPP	80	Arranged		C; 10 days	Nil
Laboratory Methods in the Diagnosis of Leptospirosis (8.53)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 2	IC	Lab, EPP	40-100	Arranged		C; 5 to 20 days	Nil
atory Methods in the Diagnosis Malaria (8.05)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 2	IC	Lab, EPP	80	Arranged		C; 10 days	Nil
Phage Typing of Salmonella Typhosa (8.52)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 2	IC	Lab, EPP	40	Arranged		C; 5 days	Nil
Serologic Differentiation of Streptococci (8.51)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 2	IC	Lab, EPP	80	Arranged		C; 10 days	Nil
Special Problems in Enteric Bacteriology (8.54)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 3	IC	Lab, EPP	80	Arranged		C; 10 days	Nil

Key will be found on page 1954.

CLINICAL PATHOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Special Training in Virus Techniques (8.21)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.; course at Communicable Disease Center, U.S.P.H.S., Virus and Rickettsia Laboratories, Montgomery, Ala.	Lab Technicians but open to MD's Lim 4	IC	Lab, EPP	80-160	Arranged		C; 10 to 20 days	Nil
Typing of Corynebacterium Diphtheriae (8.42)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 2	IC	Lab, EPP	40	Arranged		C; 5 days	Nil
Laboratory Methods in the Diagnosis of Intestinal Parasitic Diseases (8.00)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 20	IC	Lab, Lec, O, AV, EPP	160	9/15/58	10/10/58	C; 20 days	Nil
Laboratory Methods in the Diagnosis of Rabies (8.26)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 15	IC	Lab, Lec, O, AV, EPP	40	10/ 6/58 1/12/59	10/10/58	C; 5 days	Nil
Laboratory Methods in the Diagnosis of Blood Parasitic Diseases (8.01)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 20	IC	Lab, Lec, O, AV, EPP	120	10/13/58	10/31/58	C; 15 days	Nil
Laboratory Methods in the Diagnosis of Viral and Rickettsial Diseases (8.20)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.; course at Communicable Disease Center, U.S.P.H.S., Virus and Rickettsia Laboratories, Montgomery, Ala.	Lab Technicians but open to MD's Lim 12	IC	Lab, Lec, O, AV, EPP	80	10/13/58 3/ 9/59	10/24/58	C; 10 days	Nil
Laboratory Diagnosis of Viral and Rickettsial Diseases (8.20)	Communicable Disease Center, Laboratory Training Services P. O. Box 185, Chamblee, Ga.; course at CDC, Virus & Rickettsia Section, Montgomery, Ala.	G Lim 16	IC	Lab, Sem, Lec, O, AV, EPP	108	10/13/58	10/24/58	C; 12 days	Nil
Laboratory Methods in the Diagnosis of Tuberculosis (8.55)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 15	IC	Lab, Lec, O, AV, EPP	80	10/20/58 1/26/59	10/31/58	C; 10 days	Nil
Laboratory Methods in Medical Mycology (8.15)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 22	IC	Lab, Lec, O, AV, EPP	160	1/ 5/59	1/30/59	C; 20 days	Nil
Laboratory Methods in the Study of Pulmonary Mycoses (8.17)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 22	IC	Lab, Lec, O, AV, EPP	80	2/ 9/59	2/20/59	C; 10 days	Nil
Serologic Methods in Microbiology (9.41)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 10	IC	Lab, Lec, O, AV, EPP	120	3/16/59	4/ 3/59	C; 15 days	Nil
Laboratory Methods in the Diagnosis of Bacterial Diseases (8.40)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 20	IC	Lab, Lec, O, AV, EPP	80	3/ 2/59	3/13/59	C; 10 days	Nil
Laboratory Methods in the Diagnosis of Bacterial Diseases (8.41)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 20	IC	Lab, Lec, O, AV, EPP	80	3/16/59	3/27/59	C; 10 days	Nil
Laboratory Methods in the Diagnosis of Enteric Bacterial Diseases (8.50)	Communicable Disease Center U.S.P.H.S. P. O. Box 185, Chamblee, Ga.	Lab Technicians but open to MD's Lim 20	IC	Lab, Lec, O, AV, EPP	80	3/30/59	4/10/59	C; 10 days	Nil

DERMATOLOGY

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Dermatology for the General Practitioner #843	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	IC	Pd, LC, Lec, Pan, O	23	Spring/59		C; 3 days	37
Postgraduate Clinics in Dermatology	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 60	IC	PD, Lec, Pan, O, AV	14	1/16/59	1/17/59	C; 2 days	40
Dermatology for General Practitioners	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	PD, Lec, Pan, O, AV	20	7/59	7/59	C; 3 days	30
Clinical Dermatology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago [illegible]	G Lim 9	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O	120	Arranged by appointment	4 wk. 1	24 days	125

Course II in Dermatology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 15	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O	65	11/ 3/58 5/ 4/59	11/14/58	C; 12 days	100
Dermatology and Syphilology 1	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	S Lim 6	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	35-40 hr. wk.	10/ 1/58	9/30/59	C; 11 mo.	800
Dermatology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	15	10/23/58	10/25/58	C; 3 days	40
Dermatopathology	Passaic General Hospital 350 Blvd., Passaic, N.J.	B	II	Lab, Lec, O, AV	20	9/58	6/59	I; 10 sessions 2 hr. once a mo., Sundays	20
Dermatology PM 60	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	Lab, PD, Lec, O, AV, EPP	18	1/ 5/59	3/ 2/59	I; 9 sessions 2 hr. weekly, Mondays	40
521-A. Comprehensive Review in Dermatologic Histopathology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 15	IC	Lab, Sem, Surg, Lec, Pan, O, AV	35	9/ 8/58	9/12/58	C; 5 days	100
524-A. Dermatology and Syphilology for Pediatricians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV	35	10/ 6/58	10/10/58	C; 5 days	100
522-A. Seminar in Dermatology and Syphilology for General Physicians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, LC, Clin C, Sem, Surg, Lec, Pan, O, AV	35	2/16/59	2/20/59	C; 5 days	100
523-A. Symposium on Dermatology and Syphilology for Dermatologists	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 30	IC	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV	35	5/18/59	5/22/59	C; 5 days	125
Dermatology	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 5	II	PD, LC, Surg, O, EPP	20	10/ 9/58	12/18/58	I; 10 sessions 2 hr. weekly, Thursdays	85
Dermatology for Medical Practitioners	Skin and Cancer Unit of Temple University Medical Center 804 Pine St., Philadelphia 7	G Lim 20	II	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	30	10/28/58	11/25/58	I; 10 sessions 3 hr. weekly, Tuesdays	100
Postgraduate Course in Dermatologic Pathology	Skin and Cancer Unit of Temple University Medical Center 804 Pine St., Philadelphia 7	S Lim 20	IC	Lab, Clin C, Sem, Lec, O, AV, EPP	40	2/23/59	2/27/59	C; 5 days	100
Postgraduate Course in Pediatric Dermatology	Skin and Cancer Unit of Temple University Medical Center 804 Pine St., Philadelphia 7	S Lim 20	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, AV	40	4/27/59	5/ 1/59	C; 5 days	100
Dermatology for the Internist and General Practitioner	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	B	II	Lec, O, AV	15	1/59	4/59	I; Unknown	25

ELECTROCARDIOGRAPHY

(See also Cardiovascular Disease, Internal Medicine)

835—Basic Home Course in Electrocardiography	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	HS (C)	HS (C)	52	9/29/58 12/ 1/58			100
836—Advanced Home Course in Electrocardiography	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	HS (C)	HS (C)	52	9/29/58 12/ 1/58			85
Fundamentals of Electrocardiography	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	G	II	Lec		9/58	12/58	I; once weekly for 11 wk.	10
Basic Electrocardiography	Memorial Hospital 1501 Van Buren St., Wilmington 6, Del.	G	II	Lec	12	1/59	4/59	I; 12 sessions 1 hr. weekly, Wednesdays	Nil
Part I. Spatial Vector Electrocardiography; Part II. Arrhythmias	Georgetown University Medical School Washington 7, D.C.	G Lim 250	II	PD, LC, Clin C, Lec, O, AV	22½	2/ 2/59	4/ 9/59	I; 15 sessions 1½ hr. twice weekly, Mondays Thursdays	Nil
1) Basic Electrocardiography; 2) Electrocardiogram of Myocardial Infarction	Mt. Sinai Hospital of Greater Miami 4300 Alton Rd., Miami Beach 40, Fla.	G Lim 30	IC	Lec	24	9/29/58	12/19/58	I; 24 sessions 1 hr. weekly, Mondays	25
Electrocardiography and Heart Disease	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 30	IC	Lab, PD, LC, BR, Lec, O, AV, EPP	70	10/ 6/58 3/16/59	10/17/58	C; 11 days	150
One Week Advanced Course in Electrocardiography	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 30	IC	Lab, Lec, AV, EPP	40	6/15/59	6/20/59	C; 5 days	100
Electrocardiographic Interpretation	Michael Reese Hospital, Cardiovascular Dept. 29th St. and Ellis Ave., Chicago	G	IC	Sem, Lec, O, EPP	80	8/18/58	8/30/58	C; 12 days	150

Key will be found on page 1954.

ELECTROCARDIOGRAPHY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Interpretation of Complex Arrhythmias	Michael Reese Hospital, Cardiovascular Dept. 29th St. and Ellis Ave., Chicago	G Lim 20	IC	Sem, O, AV, EPP	30	12/ 8/58	12/12/58	C; 5 days	100
Basic Electrocardiography	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G Lim 30	IC	Lec, Pan, O, AV	21	9/17/58	9/19/58	C; 3 days	30
Interpretation of Electrocardiograms—I	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	HS (C), EPP	13	10/ 3/58 3/27/59	3/27/59	26 weekly lessons	25
Interpretation of Electrocardiograms—II	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	HS	HS (O), EPP	13	10/30/58 4/23/59	4/23/59	26 weekly lessons	17
Electrocardiography	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Sem, Lec, Pan, O, AV	14	2/23/59	2/24/59	C; 2 days	30
Medicine—Electrocardiography	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 60	IC	Lab, Sem, Lec	80	12/ 1/58	12/12/58	C; 10 days	100
Electrocardiography and Vectorcardiography	Heart Station, Prince Georges General Hospital Cheverly, Md.	G Lim 15	II	Lab, Clin C, Sem, Lec, O, EPP	35	10/31/58 Additional dates by arrangement	1/30/59	I; 18 to 20 sessions, 2 hr. weekly, Fridays	35
Practical Electrocardiography Course	Beth Israel Hospital 330 Brookline Ave., Boston	G Lim 35	II	Clin C, Lec, Pan, O, AV	30	10/ 1/58 3/ 4/59	12/10/58	I; 10 sessions 3 hr. weekly, Wednesdays	100
Practical Electrocardiography Course	Beth Israel Hospital 330 Brookline Ave., Boston	G Lim 35	IC	Clin C, Lec, Pan, O, AV	30	11/ 3/58 4/20/59	11/ 7/58	C; 5 days	100
Advanced Clinical Electrocardiography	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Peter Bent Brigham Hospital, Boston	S Lim 50	IC	Lab, Clin C, Lec	38	7/ 6/59	7/11/59	C; 6 days	100
Electrocardiography I	New England Center Hospital 171 Harrison Ave., Boston	G Lim 35	IC	Clin C, Sem, Lec, Pan, O, AV	30	12/ 1/58	12/5/58	C; 5 days	40
Electrocardiography II—Advanced	New England Center Hospital 171 Harrison Ave., Boston	G	IC	Sem, Lec, Pan, O	15	5/11/59	5/13/59	C; 3 days	25
Electrocardiographic Diagnosis	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	Lab, PD, Clin C, Lec, Pan, O, AV	39	4/13/59	4/18/59	C; 5½ days	75
Basic Electrocardiography	Highland Park General Hospital 369 Glendale Ave., Highland Park, Mich.	S Lim 30	II	PD, LC, Lec, O, AV, EPP	22	10/ 1/58	3/15/59	I; 22 sessions 1 hr. weekly, Fridays	Unknown
Introduction to Electrocardiography for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV, EPP	30	5/11/59	5/15/59	C; 5 days	65
Electrocardiography	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha 5	G	IC	Lec, O, AV	18	9/29/58	10/ 1/58	C; 3 days	30
Advanced Electrocardiography	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Alexian Brothers Hospital, Elizabeth, N.J.	G Lim 45	II	Lec, O, AV	16½	10/ 6/58	12/15/58	I; 11 sessions 1½ hr. weekly, Mondays	35
Clinical Correlation of Electrocardiograms with Disease Processes (Hospitalized Patients)	Albany Medical College 47 New Scotland Ave., Albany 8, N.Y.	G	II	EPP	24	Arranged		Arranged	60
Principles of Electrocardiography	Albany Medical College 47 New Scotland Ave., Albany 8, N.Y.	G	II	Sem, O, AV	12	9/18/58	10/23/58	I; 6 sessions 2 hr. weekly, Thursdays	60
Advanced Course in Interpretation of Electrocardiograms	Albany Medical College 47 New Scotland Ave., Albany 8, N.Y.	G Lim 20	II	Sem, O, AV	12	10/30/58	12/11/58	I; 6 sessions 2 hr. weekly, Thursdays	60
Electrocardiography	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	Sem, Lec, Pan, O, AV	21	11/19/58	11/21/58	C; 3 days	45
Advanced Reading Course in Electrocardiography	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N.Y.; course at Meadowbrook Hospital, East Meadow, N.Y.	G Lim 25	II	Lec	12	10/ 1/58	12/17/58	I; 12 sessions 1 hr. weekly, Wednesdays	25
Fundamentals of Electrocardiography	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N.Y.; course at Meadowbrook Hospital, East Meadow, N.Y.	G Lim 25	II	Lec	15	1/21/59	4/29/59	I; 15 sessions 1 hr. weekly, Wednesdays	25

Basic Electrocardiography	Joint Committee on Post Graduate Education 183 Bedford Ave, Brooklyn, N Y course at Beth El Hospital, Brooklyn, N Y	G Lim [illegible]	II	Lec, O, AV	[illegible]	10/58	11/58	I, [illegible] sessions 1 hr twice weekly, Mondays, Fridays	[illegible]
Medicine PM 63A—Clinical Electrocardiography	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Montefiore Hospital, New York 67	G	II	Lec, O, AV	[illegible]	9/23/58 2/3/59	1/27/59	I, 10 sessions 2 hr weekly, Tuesdays	100
Medicine PM 40—Electrocardiography	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Mount Sinai Hospital, New York 29	G	IC	Lab, PD, Lec, O, AV	30	10/13/58	10/24/58	C, 10 days	75
Medicine PM 43—Special Vectorcardiography	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Hospital for Joint Diseases, New York 35	G	IC	PD, Lec, O, AV	25	12/1/58	12/5/58	C, 5 days	75
549 A Fundamentals of Clinical Electrocardiographic Interpretation	New York University Post Graduate Medical School 550 First Ave, New York 16	G	II	Lab, Lec, O	32	11/5/58	3/4/59	I; 16 sessions 2 hr weekly, Wednesdays	55
541 A Electrocardiography	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 40	IC	PD, Lec, O, AV	25	11/12/58 3/16/59	11/15/58	C, 4 days	65
529 A Clinical Electrocardiography	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 40	II	PD, Lec, O, AV	12	4/9/59	4/28/59	I, 8 sessions 1½ hr weekly, Thursdays	45
531 A The Physiological Basis of Clinical Electrocardiology	New York University Post Graduate Medical School 550 First Ave, New York 16	G	IC	Lab, Lec, O	32	6/1/59	6/5/59	C, 4½ days	75
Fundamentals and Review Course in Electrocardiography	Westchester Heart Association, Inc Pforzheimer Memorial Bldg, Purchase, N Y	G	II	Lec, Pan, O, AV	15	10/23/58	3/10/59	I, 10 sessions 1½ hr Thursdays	
Electrocardiographic Interpretation	State University of New York Upstate Medical Center 766 Irving Ave, Syracuse, N Y	G Lim 40	II	Lab, Lec, O, AV, LPP	14	10/9/58	11/20/58	I, 7 sessions 2 hr weekly, Thursdays	15
Basic Principles of Electrocardiography	State University of New York Upstate Medical Center 766 Irving Ave, Syracuse, N Y	G Lim 7	II	Lab, Lec, AV	14	4/2/59	5/21/59	I; 7 sessions 2 hr weekly, Thursdays	15
Electrocardiographic Review, Advanced	Duke University School of Medicine Durham, N C	G Lim 40	IC	Lab, PD, LC, BR, Lec, Pan, O	18	1/59		C, 3 days	100 Paid by N C Health Dept
Electrocardiographic Review, Primary	Duke University School of Medicine Durham, N C	G Lim 40	IC	Lab, PD, LC, BR, Lec, Pan, O	18	6/59		C; 3 days	100 Paid by N C Health Dept
Advanced Electrocardiography	University of Oklahoma Medical Center 801 N E 13th St, Oklahoma City	G	IC	Lab, Sem, Lec, O, AV, LPP	40	3/2/59	3/6/59	C; 5 days	75
Basic Electrocardiography	Albert Einstein Medical Center Southern Division Fifth and Reed Sts, Philadelphia 47	G Lim 40	II	PD, Lec, AV	36	11/5/58	2/4/59	I; 12 sessions 3 hr weekly, Wednesdays	50
Advanced Electrocardiography	Albert Einstein Medical Center Southern Division *Fifth and Reed Sts, Philadelphia 47*	G Lim 15	II	Lab, PD, Lec, LPP	30	2/18/59	4/22/59	I; 10 sessions 3 hr weekly, Wednesdays	50
Electrocardiography and Other Graphic Methods in Cardiovascular Diagnosis	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg, Philadelphia	G Lim 100	II	Lec, Pan, O, AV	30	1/8/59	3/12/59	I, 10 sessions 3 hr weekly, Wednesdays	75
Electrocardiology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex; course at St Joseph's Hospital Houston, Tex	B	II	Lab, PD, BR, Clin C, Lec, AV, LPP	20	10/7/58	12/9/58	I, 10 sessions 2 hr weekly, Tuesdays	30

ELECTROENCEPHALOGRAPHY

Electroencephalography	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn; course at Yale University School of Medicine, New Haven, Conn	S Lim 10	II	Lec, O	6	10/20/58	11/3/58	I, 6 sessions 1 hr weekly, Mondays	Nil

Key will be found on page 1954.

ELECTROENCEPHALOGRAPHY - Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Neurology PM 33—Clinical Electroencephalography	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	II	Lec, O, AV	45	9/25/58	1/22/59	I; 15 sessions 3 hr. weekly	100
642-A. Electroencephalography	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 6	IC	Lab		Arranged		Arranged	350
556-A Electroencephalography	New York University Post-Graduate Medical School 550 First Ave , New York 16	G Lim 20	II	Lec, O, AV	12	10/6/58 3/ 2/59	11/24/58	I; 8 sessions 1½ hr. weekly, Mondays	35

ENDOCRINOLOGY

(See also General Practice, Gynecology, Internal Medicine, Pediatrics)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Physiological and Clinical Aspects of the Endocrine System	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	6	12/10/58	12/10/58	C; 1 day	20
West Coast Circuit Courses	California Medical Association 2975 Wilshire Blvd., Los Angeles; course at hospitals in San Luis Obispo, Santa Marie, and Santa Barbara, Calif.	G	CC	BR, Lec, Pan, O, AV, EPP	7	10/14/58	10/16/58	1 day in each town	15
Endocrinology	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	G	II	Lec		1/59	3/59	I; once weekly for 11 wk.	10
Endocrinology and Metabolism	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Sem, Lec, Pan, O, AV	14	1/28/59	1/29/59	C; 2 days	30
Recent Advances in Endocrinology	St. Michael's Hospital 306 High St., Newark, N. J.	G Lim 50	II	PD, Clin C, Lec, O, AV	8	10/58	2/59	I; 4 sessions 2 hr. mo., Wednesdays	25
Recent Advances in Endocrinology	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O	6	1/29/59	1/29/59	C; 1 day	12
Metabolic Endocrinology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Maimonides Hospital, Brooklyn, N. Y.	G Lim 20	II	PD, Lec, O	15	10/58	12/58	I; 10 sessions 1½ hr. weekly, Tuesdays	20
Endocrinology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Hospital of Brooklyn, Brooklyn, N. Y.	G Lim 15	II	Lec	12	4/59	6/59	I; 12 sessions 1 hr. weekly, Thursdays	20
5421-A. Endocrinology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	II	PD, Lec, Pan, O	24	4/ 6/59	5/29/59	I; 24 sessions 1 hr. thrice weekly, Mondays, Thursdays, Fridays	50
Endocrine Postgraduate Assembly	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	B	IC	Lec		9/29/58	10/ 2/58	C; 4 days	100

ENDOSCOPY

(See also Gastroenterology, Gynecology, Urology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Ten-Day Practical Course in Cystoscopy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 2	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, EPP	30	9/ 8/58 9/22/58 10/27/58 11/10/58 12/ 1/58 1/ 5/59 1/19/59 2/ 2/59 2/16/59 3/ 2/59 3/16/59 3/30/59 5/ 4/59 5/18/59 6/ 1/59 6/15/59 7/ 6/59 7/20/59 [illegible]	9/19/58	C; 10 days	150

Clinical Bronchoscopy	*Cook County Graduate School of Medicine* *707 S. Wood St., Chicago 12*	*G* *Lim 2*	*IC*	Lab, PD, LC, Surg, Lec, O, EPP	16	9/15/58 10/20/58 11/17/58 12/ 8/58 1/19/59 2/16/59 3/16/59 4/20/59 5/18/59 6/15/59	9/19/58	C; 5 days	100
Bronchoesophagology	University of Illinois College of Medicine 1853 W. Polk St., Chicago 12	S Lim 15	IC	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, O, AV, EPP	84	10/27/58 Spring/59	11/8/58	C; 12 days	210
Gastroscopy	*Joint Committee on Post Graduate Education* *1313 Bedford Ave., Brooklyn, N. Y.;* course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 4	II	Lec, AV	9	1/59	5/59	I; 6 sessions 1½ hr. weekly, Mondays	30
Bronchoscopy (Cadaver demonstrations)	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 8	II	Lab, Lec, O		Arranged		I; 8 sessions 1 hr. each, Wednesdays	150
Culdoscopy	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 8	II	PD, Lec	6	10/ 1/58 4/ 1/59	10/31/58	I; 3 sessions 2 hr. each, Monday, Wednesday, Friday	100
513-A. Gastroscopy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 2	II	Lab, PD, EPP	36	9/ 8/58 12/ 1/58	12/ 8/58	I; 36 sessions 1 hr. thrice Weekly, Mondays, Wednesdays, Fridays	300
566 A. Culdoscopy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 4	II	PD, LC, Surg, Lec, O, AV	6	11/24/58 1/26/59 4/27/59	11/28/58	I; 3 sessions 2 hr. each Monday, Wednesday, Friday	55
595-A. Endoscopy; Bronchoesophagology and Laryngology	New York University Post Graduate Medical School 550 First Ave., New York 16	S Lim 10	IC	Lab, PD, LC, Sem, Surg, Lec, O, EPP	12	12/ 1/58	12/ 5/58	C; 6 days	100
Bronchoesophagology—Diagnosis and Treatment of Diseases of Bronchi, Lungs and Esophagus	*Chevalier Jackson Clinic, Temple University Medical Center* 3401 N. Broad St., Philadelphia 40	B Lim 21	IC	Lab, PD, LC, Clin C, Sem, Surg, Pan, O, AV	80	11/ 3/58 Spring/59	11/14/58	C; 11 days	250

EPHEBOLOGY

(See also Internal Medicine, Pediatrics, Psychiatry)

Medical Alumni Seminar—A New Look at Adolescence and Problems	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Children's Hospital, San Francisco	G	IC	Clin C, Sem, Pan, O, AV	7	11/15/58 1/24/59	11/15/58	C; 1 day	12.50
Adolescent Medicine 1	Harvard Medical School, Courses for Graduates 25 Shattuck St., *Boston 15;* course at Children's Hospital, Boston	G Lim 2	IC	PD, LC, BR, Clin C, Sem, Lec	35-40 hr. wk.	*Arranged*		*Arranged*	300

FORENSIC MEDICINE

(See also Occupational Medicine)

Forensic Pathology	*Armed Forces Institute of Pathology* 6825 - 16th St., N.W., Washington 12, D. C.	S Lim 60	IC	*Lab*, Sem, Lec, *Pan*, O, AV, TV	10	10/ 6/58	10/11/58	C; 5½ days	Nil
513-A. Toxicology	New York University Post-Graduate Medical School 650 First Ave., New York 16	G and non-Physicians Lim 6	IC	Lab, Sem, Lec, AV, EPP		Arranged		Arranged	100 per mo.
Compensation and Public Liability	Rochester General Hospital 501 W. Main St., Rochester, N. Y.	G	IC	Clin C, Sem, Pan, AV	12	11/11/58	11/13/58	C; 3 days	30

FRACTURES

(See also General Practice, Orthopedic Surgery, Radiology, Surgery)

Fractures	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV		12/ 5/58	12/ 6/58	C; 2 days	Unknown
Course II in Clinical Fractures	Cook County Graduate School of Medicine *707 S. Wood St., Chicago 12*	G Lim 3	PT	PD, LC, BR, Clin C, Surg, Lec, O	35	Arranged by appointment	Saturday following starting date	5 days	50

Key will be found on page 1954.

FRACTURES—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Course III in Fractures and Traumatic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	80	10/20/58 3/ 9/59 6/15/59	11/ 1/58	C; 12 days	150
Fractures	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IC	PD, Lec, Pan, O, AV	14	11/17/58	11/18/58	C; 2 days	30
Treatment of Fractures and Other Traumatic Conditions	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	G Lim 75	IO	PD, LC, Lec, Pan	46	9/29/58	10/ 4/58	C; 6 days	150
Fractures for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	18	11/17/58	11/19/58	C; 3 days	40
Course in Fractures	Duke University School of Medicine Durham, N. C.	G	IC	Unknown	4	10/ 4/58	10/ 4/58	C; 1 day	Unknown
Fractures	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	G Lim 270	II	PD, Lec, Pan	9	5/ 5/59	5/19/59	I; 3 sessions 3 hr. weekly, Tuesdays	20

GASTROENTEROLOGY

(See also Basic Sciences, Endoscopy, Radiology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Physiological and Clinical Aspects of the Gastrointestinal Tract	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	6	2/18/59	2/18/59	C; 1 day	20
Gastroscopy and Gastroenterology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 5	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV, EPP	40	9/ 8/58 3/ 2/59	9/19/58	C; 12 days	200
Gastroenterology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, O	60	4/13/59	4/24/59	C; 12 days	150
Diarrheal Diseases	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	11	1/21/59	1/22/59	C; 2 days	15
Clinical Traineeship in Gastroenterology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, AV, EPP		Arranged	1 mo. later	30 days	50 per mo. in state; 100 per mo. out of state
Gastroenterology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, Pan, O, AV	14	1/21/59	1/22/59	C; 2 days	45
Gastroenterology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	B Lim 150	IC	PD, Lec, Pan, O, AV	35	11/10/58	11/14/58	C; 5 days	50
Modern Concepts in Gastroenterology	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Clara Maass Memorial Hospital, Belleville, N. J.	G Lim 50	II	Lec, O, AV	18	1/15/59	4/ 9/59	I; 12 sessions 1½ hr. weekly, Thursdays	60
Diagnosis and Treatment of Diseases of the Colon	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 8	II	Lec, AV	9	10/58	11/58	I; 6 sessions 1½ hr. weekly, Mondays	20
Postgraduate Gastroenterology	American College of Gastroenterology 33 W. 60th St., New York 23; course at Jung Hotel, New Orleans	B	IC	LC, Lec	18	10/23/58	10/25/58	C; 3 days	35 for members; 50 non-members
Medicine PM 70-Gastroenterology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 30	II	PD, Lec, O, AV	52½	9/ 9/58	12/16/58	I; 15 sessions 3½ hr. weekly, Tuesdays	75
Medicine PM 73 Advanced Gastroenterology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	Sem, Lec, O, AV	52½	1/13/59	4/28/59	I; 15 sessions 3½ hr. weekly, Tuesdays	75
Medicine PM 45 Gastroenterology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York	G	IC	PD, LC, BR, Lec, O, AV	30	4/ 6/59	4/10/59	C; 5 days	75

Clinical Gastroenterology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lee, O	60	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	75
5428 A. Gastroenterology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 15	II	PD, LC, Clin C, Lee, Pan, O	24	4/ 8/59	4/27/59	I; 8 sessions 3 hr. weekly, Wednesdays	40
5436-A. Clinical Gastroenterology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 10	IC	PD, LC, Clin C, Lee, Pan, O	35	6/22/59	6/26/59	C; 5 days	75
Seminar on Diseases of the Digestive Tract	Ohio Academy of General Practice 209 S. High St., Columbus 15, Ohio; course at Good Samaritan Hospital, Dayton, Ohio	G	II	Sem	20	9/ 4/58	11/ 5/58	I; 10 sessions 2 hr. weekly, Thursdays	Unknown
Seminar on Gastrointestinal Disease	Dr. Gaston B. Hannah Southwestern Ohio Society of General Physicians Sharon and Willow Aves., Glendale, O.; course at Hartwell Country Club, Cincinnati	G	IC	Lee, Pan	4	10/19/58	10/19/58	C; 1 day	10
Gastroenterology	American College of Physicians 4200 Pine St., Philadelphia 4; course at University of Michigan Medical School, Ann Arbor, Mich	S	IC	Clin C, Lee, Pan, O, AV	35-40	11/10/58	11/14/58	C; 5 days	30 A. C. P. members; 60 non-members
Special Diagnostic Methods and Procedures in Gastroenterology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G	II	Lee, Pan, O, AV	16	9/58	5/59	I; 16 sessions 1 hr. weekly, Fridays	30
Conference in Gastroenterology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab Bldg., Philadelphia	B Lim 10	II	Lee, O, AV	60	9/58	5/59	I; 30 sessions 2 hr. weekly, Thursdays	50

GENERAL PRACTICE

(See also all other categories)

Postgraduate Medical Assembly—Internal Medicine and Surgery	Birmingham Academy of Medicine Tutwiler Hotel, Birmingham, Ala.	G Lim 500	IC	Clin C, Sem, Lee, Pan, AV	21	9/ 7/58	9/ 9/58	C; 3 days	15
John A. Andrew Clinical Society	Secretary, John A Andrew Memorial Hospital of Tuskegee Institute Tuskegee Institute, Ala.	G Lim 500	IC	Lab, PD, LC, BR, Clin C, Sem, Lee, Pan, O, AV	30	4/12/59	4/17/59	C; 6 days	15
North Coast Counties Circuit Course	California Medical Association 2975 Wilshire Blvd., Los Angeles; course at hospitals in Eureka, Ukiah, Napa, Calif.	G	CC	Lee, O	16	10/ 3/58	3/27/59	Mondays, Tuesdays and Wednesdays	30
Sacramento Valley Circuit Courses—6th Annual	California Medical Association 2975 Wilshire Blvd., Los Angeles; course at Marysville and Auburn, Calif.	G	CC	LC, BR, Lee, O	32	10/13/58	3/27/59	1 weekly; 8 sessions (4 hr.)	30
Sacramento Valley Circuit Courses—6th Annual	Dunsmuir and Chico, Calif.	G	CC	Lee	16	10/13/58	3/27/59	1 weekly; 8 sessions (2 hr.)	30
9th Annual Regional Postgraduate Institute—North Coast Counties	California Medical Association 2975 Wilshire Blvd., Los Angeles; course at Hoberg's Resort, Lake County, Calif.	G	IC	Lab, LC, Sem, Lee, Pan, O, EPP	12	6/ 4/59	6/ 6/59	C; 3 days	20
9th Annual Regional Postgraduate Institute—Southern Counties	California Medical Association 2975 Wilshire Blvd., Los Angeles 5; course at Disneyland Hotel, Anaheim, Calif.	G	IC	Sem, Lee, Pan, O	12	4/23/59	4/24/59	C; 2 days	20
9th Annual Regional Postgraduate Institute—West Coast Counties	California Medical Association 2975 Wilshire Blvd , Los Angeles 5; course at Golden Bough Theater and La Playa Hotel, Carmel, Calif.	G	IC	PD, Sem, Lee, Pan, O, AV	12	5/14/59	5/15/59	C; 2 days	20
9th Annual Regional Postgraduate Institute—Sacramento Valley Counties	California Medical Association 2975 Wilshire Blvd., Los Angeles; course at Tahoe Tavern, Lake Tahoe, Calif.	G	IC	Lee, Pan, O	12	6/25/59	6/27/59	C; 3 days	20
Stockton Postgraduate Study Club	Stockton Post Graduate Study Club 936 N. Commerce St., Stockton, Calif.; course at College of the Pacific, Stockton, Calif.	G	II	Lee, Pan, O, AV	12	9/11/58	11/13/58	I; 8 sessions 1½ hr. weekly, Thursdays	10
Postgraduate Medical Lecture Series	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24; course at St. Joseph Hospital, Burbank, Calif.	G Lim 10	II	Sem, Lee, Pan, O, AV	24	9/23/58	12/ 9/58	I; 12 sessions 2 hr. weekly, Tuesdays	50

Key will be found on page 1934.

GENERAL PRACTICE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Medical Lecture Series	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24; course at St. Mary's Hospital, Long Beach, Calif.	G	II	Lec, Pan, O, AV	24	3/ 3/59	5/19/59	I; 12 sessions 2 hr. weekly, Tuesdays	50
Common Problems of the Foot	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	PD, Sem, Lec, Pan, O, AV		Spring/59		Unknown	Unknown
Management of Non-Surgical Emergencies	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV		Spring/59		Unknown	Unknown
849—Symposium on Sexual Problems as Seen in General Practice	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Statler Hotel, Los Angeles	G	IC	Lec, Pan, O, AV	7	11/ 7/58	11/ 7/58	C; 1 day	25
852—Ward Walks in Rare Diseases	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Los Angeles County Hospital, Los Angeles 33	G Lim 20	II	PD, LC, BR, Lec, Pan	24	Spring/59		I; 12 sessions 2 hr. weekly, Thursdays	65
Twelfth Postgraduate Assembly	San Diego County General Hospital North end of Front St., San Diego 3, Calif.	B Lim 400	IC	Sem, Lec, Pan, AV	12	9/17/58	9/18/58	C; 1½ days	Nil
Medicine for General Practitioners	University of California Medical Center Second and Parnassus Ave., San Francisco; course at East Oakland Hospital, Oakland, Calif.	G Lim 50	II	Lec	24	9/16/58	12/ 9/58	I; 12 sessions 2 hr. weekly, Tuesdays	50
Medical Alumni Seminar—A New Look at Vaccination and Immunity	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Children's Hospital, San Francisco	G	IC	Clin C, Sem, Pan, O, AV	7	3/21/59	3/21/59	C; 1 day	12.50
Course for Physicians in General Practice	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Mt. Zion Hospital, San Francisco	G Lim 100	IC	Lab, PD, Clin C, Lec, Pan, O, AV	35	4/ 6/59	4/10/59	C; 5 days	70
Saint John's Hospital Postgraduate Assembly	Dr. John C. Eagan, Director Postgraduate Assembly, Saint John's Hospital 1328 22nd St., Santa Monica, Calif.	G Lim 600	IC	Lab, LC, Clin C, Lec, Pan, O	28	9/11/58	9/13/58	C; 3 days	Nil
General Applied Medical Science	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20; course at Fitzsimons Army Hospital Denver, Colo.	G	II	Lec		9/58	4/59	I; once weekly, Thursdays for 8 mo.	10
General Practice Review	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	G	IC	PD, Lec, O, AV	45	1/19/59	1/24/59	C; 6 days	55
Summer School of Alcohol Studies	Yale University Summer School of Alcohol Studies 52 Hillhouse Ave., Yale Station, New Haven, Conn.	G and non-medical persons	O	PD, Sem, Lec, Pan, O, AV	74	6/29/59	7/24/59	22 days	250
Management of Mass Casualties	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	G Lim 150	IC	Sem, Lec, Pan, O, AV, TV	44	9/15/58 2/16/59	9/20/58	C; 6 days	Nil
Management of Mass Casualties	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Brooke Army Medical Center, Ft. Sam Houston, Tex.	G Lim 120	IO	Sem, Lec, Pan, O, AV	40	9/22/58 12/ 1/58 2/ 9/59 4/27/59 6/15/59	9/26/58	C; 5 days	Nil
Principles of Medical Operations in Nuclear Warfare	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.;	G Restricted to military personnel Lim 24	IO	Lec, Pan, O, AV, TV		9/29/58 3/23/59	10/31/58	C; 33 days	Nil
							5/ 9/59	C; 3 days	20

[illegible]	[illegible] 707 S. Wood St., Chicago 12	[illegible] Lim 12	[illegible]	[illegible], PD, LC, Surg, Lec, O	10	9/15/58 2/ 2/59 3/ 2/59 4/ 6/59 5/ 4/59 6/ 1/59	9/17/58	C; 2 days	60
Medicine for Today	Illinois Academy of General Practice 14 E. Jackson Blvd., Chicago 4; course at Alton, Belleville, Centralia, Chicago (North), Chicago (South), Chicago Heights, Champaign, Effingham, Elgin, Elmhurst, Geneva, Herrin, Hinsdale, Joliet, Moline, Mount Carmel, Oak Park, Ottawa, Peoria, Rockford, Springfield, Waukegan	G	CO	PD, Lec, O, AV	24	9/29/58 3/16/59	11/14/58	12 sessions 2 hr. each	40 for members; 80 for non-members
General Medicine	Chicago Medical Society 86 E. Randolph St., Chicago; course at Hamilton Hotel, Chicago	G Lim 100	IO	Lec, Pan, O	29½	10/27/58	10/31/58	C; 5 days	75
Refresher Course for the General Physician	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IO	PD, BR, Lec, Pan, O, AV	28	2/17/59	2/20/59	C; 4 days	45; 3 to members of AGP
Alumni Day	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IO	Lec, Pan, O, AV	8	6/12/59	6/13/59	C; 2 half days	Nil
Infectious Diseases	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IC	Lec, Pan, O, AV	7	9/19/58	9/19/58	C; 1 day	Nil
General Practice Symposia	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	II	Lec, Pan, O, AV	24	11/20/58	4/16/59	I; 6 sessions 4 hr. once mo., Thursdays	10 members K. C. or Wyandotte Acad.; 20 non-members
Kansas Circuit Course	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.; course at Riley County Hospital, Manhattan, Ks. St. Joseph Hospital, Concordia, Ks St. Elizabeth Hospital, Hutchinson, Ks. Colby Country Club, Colby, Ks To be selected, Arkansas City, Ks. To be selected, Garden City, Ks Newman Memorial Hospital, Emporia, Ks St. Rose Hospital, Great Bend, Ks.	G	CC	PD, Lec, Pan, O, AV	33 at each location	12/ 2/58 12/ 2/58 12/ 3/58 12/ 3/58 12/ 4/58 12/ 4/58 12/ 5/58 12/ 5/58	4/28/59	5½ hr. one day a mo.; afternoon and evening for 6 mo.	30
General Medicine and Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.; course at Southeast Kansas Tuberculosis Hospital, Chanute, Ks.	G	II	Clin C, Lec, O, AV	7	Unknown		I; 7 sessions 1 hr.	Unknown
General Medicine and Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks course at St. Joseph, Mo.	G	II	Lec, O, AV	7	Unknown		I; 7 sessions 1 hr.	Nil
The Ophthalmoscope: Its Use in Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IO	PD, Lec, Pan, O, AV	7	1/23/59	1/23/59	C; 1 day	15
Fall Clinical Conference—Symposium on Gastrointestinal and Infectious Diseases	Lexington Clinic 1300 S. Broadway, Lexington, Ky.; course at hotel, Lexington, Ky.	G	IC	Lab, Clin C, Sem, Lec, Pan, O, AV	9 to 12	10/22/58	10/23/58	C; 2 days	Nil
Refresher Course for Practitioners	Louisiana State University School of Medicine 1542 Tulane Ave., New Orleans; course at Confederate Memorial Medical Center, Shreveport, La.	G Lim 150	II	PD, Clin C, Lec, Pan, O, AV	100	9/58	3/59	I; 16-17 sessions 6 hr. biweekly, Thursdays	Unknown
Postgraduate Medical Refresher Course	Medicallnics of Minnesota 601 Medical Arts Bldg., Minneapolis; course at Florida Academy of General Practice, Fort Lauderdale	G Lim 350	IC	Lec, Pan	32	3/ 2/59	3/12/59	C; 9 days	50
Neurology and Neurosurgery for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IO	Lec, O, AV	30	11/17/58	11/21/58	C; 5 days	65
The Newer Drugs in General Practice	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	15	1/15/59	1/17/59	C; 3 days	40
Trauma for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	7	3/11/59	3/11/59	C; 1 day	10
Fall Refresher	Minnesota Academy of General Practice 15 Ninth Ave., S., Hopkins, Minn.; course at Mayo Civic Auditorium, Rochester, Minn.	G	IO	PD, LC, Sem, Lec, Pan, O, AV	10	10/21/58	10/22/58	C; 2 days	10

Key will be found on page 1954.

GENERAL PRACTICE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Traineeships—Registrant chooses field	University of Mississippi Medical Center, Secretary, Postgraduate Education Committee 2500 N. State St., Jackson, Miss.	G	PT	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	Arranged	Arranged		Arranged	Nil
Annual Symposium on Infectious Diseases	American Academy of General Practice Volker Blvd. at Brookside, Kansas City, Mo.; course at Battenfeld Auditorium, University of Kansas Medical Center, Kansas City, Ks.	G	IC	Lec, Pan, O, AV	6	9/19/58	9/19/58	C; 1 day	Nil
Spring Postgraduate Conference—Surgery, Obstetrics and Gynecology	The Creighton University School of Medicine and Creighton Memorial-St. Joseph Hospital Omaha, Neb.	G Lim 50	IC	PD, LC, BR, Clin C, Lec, Pan, O	15	4/14/59	4/16/59	C; 2½ days	10
Fourth Annual Trauma Day	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Clin C, Sem, Lec, Pan, O, AV	6	5/ 6/59	5/ 6/59	C; 1 day	10
Visiting Chief Program	Atlantic City Hospital 26 S. Ohio Ave., Atlantic City, N. J.	G Lim 50	O	PD, LC, BR, Sem, Lec, O, AV	480 per year	1/ 5/59	12/19/59	C; 240 days per year	Nil
Internal Medicine and General Surgery Review	Director of Education, Lovelace Foundation 4800 Gibson Blvd., S.E., Albuquerque, N. Mex.; course at Bataan Memorial Methodist Hospital, Albuquerque, N. Mex.	G Lim 50	IC	PD, LC, BR, Clin C, Lec, Pan, O	12	10/15/58 12/10/58 2/11/59 3/25/59	10/18/58	C; 3 days	Nil
Internal Medicine and General Surgery Review	Director of Education, Lovelace Foundation 4800 Gibson Blvd., S.E., Albuquerque, N. Mex.; course at various County Medical Societies throughout state	G	CC	Lec	2	10/20/58 12/ 5/58 2/16/59 3/20/59	10/20/58	C; 1 day	Nil
Clinical Refresher Course—Choice of Subject	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 1	IC	PD, LC, BR	As desired	Arranged		As desired	60 for each 5 days
Two-Way Radio Conference—Albany Medical College to Area Hospitals	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	R	Radio lec, O	24	11/ 4/58	5/ 1/59		Nil
Prophylactic Use of Antibiotics	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	1/22/59	1/22/59	C; 1 day	12
Recent Advances in Clinical Practice	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV	39	9/ 8/58	9/13/58	C; 6 days	75
Modern Laboratory Procedures in Clinical Practice; Their Use and Interpretation	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	Lab, Sem, Lec, Pan, O	14	10/15/58	10/16/58	C; 2 days	30
Fluid and Electrolyte Therapy and Parenteral Nutrition in Medicine, Surgery and Pediatrics	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	11/12/58	11/13/58	C; 2 days	30
Minor Surgery and Office Orthopedics	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	12/10/58	12/11/58	C; 2 days	30
Postgraduate Radio Program	The New York Academy of Medicine 2 E. 103rd St., New York 29	G	HS(R)	Lec, Pan	52	9/58	9/59	I; 52 sessions 1 hr. weekly, Thursdays	Nil
Postgraduate Week, Research Contributions to Clinical Practice	The New York Academy of Medicine 2 E. 103rd St., New York 29	G Lim 700	O	Lec, Pan	18	10/13/58	10/17/58	C; 5 days	Nil
Monthly Panel Meetings on Therapeutics for the General Physician	The New York Academy of Medicine 2 E. 103rd St., New York 29	G	II	Lec	9	11/14/58	4/10/59	I; 6 sessions 1½ hr. mo., Fridays	Nil
Proctology, Gastroenterology, with Operative Proctology (cadaver)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	72	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	200
Course for General Practitioners—Medicine, Surgery, Allied Subjects	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, Pan, O, AV	192	10/ 1/58 4/ 1/59	10/31/58	C; 30 days	100
Seminar on Dyspnoea	New York Polyclinic Hospital 345 W. 50th St., New York 19	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	16	11/17/58	11/18/58	C; 2 days	35
Low Back Pain	New York Polyclinic Hospital 345 W. 50th St., New York 19	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	16	11/19/58	11/20/58	C; 2 days	35
Pain in Right Lower Quadrant	New York Polyclinic Hospital 345 W. 50th St., New York 19	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	16	11/21/58	11/22/58	C; 2 days	35
545-A. General Medicine. The Application of Recent Advances to Clinical Practice	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	Clin C, Lec, O, AV	56	9/16/58	5/12/59	I; 28 sessions 2 hr weekly, Tuesdays	200
541-A. Review Course in General Medicine	New York University Post-Graduate	G	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	70	7/ 7/59	7/18/59	C; 10 days	125

Trauma	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	B Lim 100	IC	Lec, Pan, O, AV		Spring/59		C; 1 day	Unknown
Buncombe County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine Chapel Hill, N. C.; course at Memorial Mission Hospital, Asheville, N. C.	G	II	Lec, Pan, O, AV	18	9/16/58	10/28/58	I; 6 sessions 3 hr. weekly, Tuesdays	25
Burke County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine Chapel Hill, N. C.; course at Grace Hospital, Morganton, N. C.	G	II	Lec, Pan, O, AV	18	9/17/58	10/29/58	I; 6 sessions 3 hr. weekly, Wednesdays	25
University of North Carolina School of Medicine Symposium	University of North Carolina School of Medicine Chapel Hill, N. C.	G	IC	PD, BR, Clin C, Lec, Pan, O, AV	12	11/20/58	11/21/58	C; 2 days	Nil
First District Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine Chapel Hill, N. C.; course at Edenton, Ahoskie, Elizabeth City, N. C.	G	CC	Lec, Pan, O, AV	18	1/14/59	2/18/59	I; 6 sessions 3 hr. weekly, Wednesdays	25
Wake County Postgraduate Medical Course	Office of Continuation Education University of North Carolina School of Medicine Chapel Hill, N. C.; course at Rex Hospital and Hotel Sir Walter Raleigh, Raleigh, N. C.	G	II	Lec, Pan, O, AV	18	1/15/59	2/19/59	I; 6 sessions 3 hr. weekly, Thursdays	25
Duke Medical Postgraduate Course	Duke University School of Medicine Durham, N. C.	G Lim 50	IC	Lab, PD, LC, BR, Surg, Lec	28	6/15/59	6/18/59	C; 4 days	25
Postgraduate Course in Mycology	Duke University School of Medicine Durham, N. C.	G Lim 20	IC	Lab, PD, LC, BR, Lec, Pan	84	7/ 1/59	7/31/59	C; 21 days	100
Pediatrics, Internal Medicine, Obstetrics and Gynecology	Southern Postgraduate Seminar Saluda, N. C.	G Lim 125	IC	PD, Clin C, Sem, Lec, Pan, AV	35 hr per wk	7/ 6/59	7/25/59	C; 3 wk.	35 per wk.
General Practice—Recent Advances in Specialties	Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland	G Lim 125	IC	LC, Sem, Surg, Lec, Pan, O, AV	10	2/11/59	2/12/59	C; 2 days	20
Annual Postgraduate Seminar	Huron Road Hospital 13951 Terrace Road, Cleveland 12	B Lim 150	IC	Sem, Lec, Pan, O	16	Spring 59		C; 2 days	15
Selected Topics in Medicine	Registrar, School of Medicine, Western Reserve University 2109 Adelbert Rd, Cleveland; course at University Hospitals of Cleveland, Cleveland	G Lim 80	II	PD, Clin C, Lec, Pan, O, AV	30	9/17/58	11/26/58	I; 10 sessions 3 hr. weekly, Wednesdays	30
Postgraduate Short Course Series	University of Oklahoma Medical Center 801 N. E. 13th St., Oklahoma City	G	II	PD, LC, Sem, Lec, Pan, O, AV	40	9/10/58	6/10/59	I; 10 sessions 4 hr. 2nd Wednesday of each mo.	25 for series, 3.50 per session
Oregon-Oklahoma Combined Specialty Meeting	University of Oklahoma Medical Center 801 N. E. 13th St., Oklahoma City	G	IC	Clin C, Sem, Lec, Pan, O	9	10/ 3/58	10/ 4/58	C; 2 days	15
Recent Advances in Clinical Practice	University of Oklahoma Medical Center 801 N. E. 13th St., Oklahoma City	G	IC	PD, Sem, Lec, Pan, O, AV	8	5/22/59	5/22/59	C; 1 day	Nil
Refresher Course for General Practitioners	Geisinger Memorial Hospital and Foss Clinic Danville, Pa.	G Lim 20	II	PD, LC, BR, Clin C, Sem, Surg, Lec, O, AV	60	1/14/59	3/18/59	I; 20 sessions 3 hr. weekly, Wednesdays	60
Refresher Course for General Practitioners	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 21	II	PD, LC, BR, Sem, Pan, AV, EPP	50	3/ 4/59	5/ 6/59	I; 10 sessions 5 hr. weekly, Wednesdays	50
The Jefferson Graduate Assembly	The Jefferson Medical College 1025 Walnut St., Philadelphia	G	IC	PD, LC, Clin C, Lec, Pan, O, AV	18	2/ 4/59	2/ 6/59	C; 3 days	15
Advances in Clinical Medicine	U. S. Veterans Administration Hospital University Dr., Pittsburgh	G Lim 50	II	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, AV	60	3/ 5/59	5/ 7/59	I; 10 sessions 6 hr. weekly, Thursdays	60
Greenville Post-Graduate Seminar	Greenville General Hospital 100 Mallard St., Greenville, S. C.	G	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	23	4/14/59	4/16/59	C; 3 days	Nil
Founders' Day Postgraduate Seminar	Medical College of South Carolina 16 Lucas St., Charleston, S. C.	G	IC	PD, LC, Lec, AV	22	11/ 4/58	11/ 6/58	C; 3 days	Unknown
Advanced Clinical Bedside Courses	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive, Houston 25, Tex.; course at Texas Medical Center Institutions, Houston, Tex.	G Lim 5	II	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	8	9/ 9/58 1/59	9/30/58	I; 4 sessions 2 hr. weekly, Tuesdays	15
Postgraduate Conference	University of Virginia School of Medicine Charlottesville, Va.	G	O	PD, LC, BR, Clin C, Sem, Lec, Pan, O		11/58 2/59 5/59	11/58	C; 1 day	Nil

Key will be found on page 1954.

GENERAL PRACTICE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
General Practice 1958	Assistant to the Dean University of Wisconsin Medical School 418 N. Randall Ave., Madison 6, Wis.	G Lim 100	IC	PD, Lec, Pan, O, AV	18	11/ 6/58	11/ 8/58	C; 2½ days	30

GERIATRICS

(See also Gynecology, Internal Medicine, Malignant Disease, Psychiatry)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Graduate Symposium on Geriatric Medicine	American Geriatrics Society 2907 Post Road, Greenwood, R.I.; course at Waldorf-Astoria Hotel, New York 22	G	IC	PD, Sem, Lec, Pan, O, AV	16	11/ 6/58	11/7/58	C; 2 days	Nil
Medical Problems of the Elderly	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M. D. Anderson Hospital, Houston, Tex.	B Lim 200	IC	Lec, Pan, AV	24	10/21/58	10/24/58	C; 4 days	5

GYNECOLOGY

(See also, Anatomy, Endoscopy, Pathology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Course II in Office and Operative Gynecology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 18	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	94	9/ 8/58 10/13/58 2/ 9/59 3/16/59 4/13/59 6/15/59	9/20/58	C; 12 days	150
Vaginal Approach to Pelvic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	PD, LC, BR, Surg, Lec, O, AV	20	10/ 6/58 11/17/58 2/ 2/59 3/ 9/59 4/27/59 6/ 8/59	10/10/58	C; 5 days	125
Gynecology 3	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	G Lim 30	IC	Lab, PD, LC, BR, Clin C, Lec	78	9/15/58	9/26/58	C; 11 days	175
Gynecology 4	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Free Hospital for Women, Brookline, Mass.	G Lim 45	IC	Lab, PD, Clin C, Surg, Lec, Pan	45	4/27/59	5/ 1/59	C; 5 days	100
Gynecology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G Lim 50	IC	Lec, O, AV	18	6/15/59	6/17/59	C; 3 days	40
Modern Concepts in Gynecology	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Alexian Brothers Hospital, Elizabeth, N.J.	G Lim 50	II	Lec, O, AV	15	1/ 7/59	3/11/59	I; 10 sessions 1½ hr. weekly, Wednesdays	60
Gynecology	University of Buffalo School of Medicine 3435 Main St., Buffalo	G Lim 16	IC	PD, Sem, Lec, Pan, O, AV	14	10/ 8/58	10/ 9/58	C; 2 days	30
Office Gynecology	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N.Y.; course at Meadowbrook hospital, East Meadow, N.Y.	G Lim 10	II	Lec	6	2/ 5/59	3/12/59	I; 6 sessions 1 hr. weekly, Thursdays	15
Applied Gynecological Pathology	The Long Island Jewish Hospital 270-05 76th Ave., New Hyde Park, N.Y.	S Lim 10	II	Clin C, AV	42	10/ 6/58	1/ 5/59	I; 14 sessions 3 hr. weekly, Mondays	100
Office Gynecology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Hospital of Brooklyn, Brooklyn, N. Y.	G Lim 20	II	Lec, AV	10	10/58	12/58	I; 10 sessions 1 hr. twice weekly, Mondays, Thursdays	20
500-A Diagnosis and Therapy of Malignant Neoplasms of the Female Genital Tract	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 10	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, O, AV, EPP	35	9/29/58	10/ 3/58	C; 5 days	150
505-A Gynecological Cytology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S	II	Lab, Sem, Lec, O, AV, EPP	32	9/30/58 4/14/59	11/25/58	I; 16 sessions [illegible] Tuesdays,	100

[illegible]	[illegible] Medical School 550 First Ave., New York 16	Lim 30	[illegible]	[illegible] Sem, Lec, O	[illegible]	10/ 6/58 4/ 6/59	10/10/58	C; 5 days	125
Gynecology	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N Y.	G Lim 12	IC	LC, Lec, Pan, O	40	4/20/59	4/24/59	C; 5 days	25
Clinical Gynecology—Clinical Symptomatology, Diagnosis and Management	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at University of Texas M. D Anderson Hospital, Houston, Tex.	G Lim 4	II	Lab, PD, LC, BR, Clin C, Lec, EPP	48	9/ 2/58 10/ 7/58 11/ 4/58 scheduled also for 1959	9/25/58	I; 8 sessions 6 hr. twice weekly, Tuesdays, Thursdays	50

HEMATOLOGY

(See also Internal Medicine)

Clinical Hematology	University of Colorado School of Medicine 1200 E. Ninth Ave., Denver 20	S Lim 12	IC	Lab, PD, BR, Lec, AV, EPP	48	6/59	6/59	C; 6 days	100
Hematology	Cook County Graduate School of Medicine 707 S Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, O	30	6/ 1/59	6/ 5/59	C; 5 days	100
Clinical Hematology	Indiana University School of Medicine 1100 W Michigan St., Indianapolis 7	G	II	Lab, PD, LC, BR, Clin C, O, AV	24	Any Thursday		I; 12 sessions 2 hr. weekly, Thursdays	30
Hematology—I	University of Kansas School of Medicine 39th and Rainbow Blvd., Kansas City, Ks	G	HS	HS (C), Lab, AV, EPP		10/ 1/58 4/ 1/59	6/ 1/59	9 monthly lessons	15
Clinical Traineeship in Hematology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G Lim 1	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	120	11/ 3/58 2/ 2/59 3/ 2/59	11/29/58	30 days	50 per mo. in state; 100 per mo. out of state
Hematology, Thrombosis, Embolization and Fibrinolysis	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IC	PD, Sem, Lec, Pan, O, AV	14	2/16/59	2/17/59	C; 2 days	30
Pediatric Hematology	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IC	Sem, Lec, Pan, O	20	4/ 9/59	4/11/59	C; 2½ days	25
Hematology	New England Center Hospital 171 Harrison Ave., Boston	S Lim 75	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	15	4/ 9/59	4/11/59	C; 3 days	20
Diseases of Blood and Blood forming Organs	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	G Lim 10	IC	Lab, PD, Clin C, Lec, Pan, O	35	3/30/59	4/ 3/59	C; 5 days	50
Hematology	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha 5	G	IC	Lab, Sem, Lec, Pan, O, AV, EPP	12	10/15/58	10/16/58	C; 2 days	20
Practical Aspects of Clinical Hematology	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Martland Medical Center, Newark, N J	G Lim 45	II	Lec, O, AV	15	12/22/58	3/ 4/59	I; 10 sessions 1½ hr. weekly, Wednesdays	50
Hematological Disorders—Part of course entitled "Application of Modern Medicine to Every day Practice"	Nassau Academy of Medicine, Inc 1200 Stewart Ave., Garden City, N Y; course at Doctors Hospital, Freeport, N Y	G Lim 30	II	Sem	12	9/ 2/58	10/21/58	I; 8 sessions 1½ hr. weekly, Tuesdays	21
Medicine PM 66—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 20	II	Lab, PD, BR, Lec, O, AV	72	9/ 9/58	1/20/59	I; 18 sessions 4 hr. weekly, Tuesdays	100
Medicine PM 20—Clinical Hematology	Columbia University College of Physicians and Surgeons 630 W 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lab, PD, LC, Lec, O, AV	24	10/28/58	12/16/58	I; 8 sessions 3 hr. weekly, Tuesdays	50
Medicine PM 67—Advanced Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 10	II	Lab, PD, EPP	32	2/ 3/59	5/19/59	I; 16 sessions 2 hr. weekly, Tuesdays	75
Medicine PM 21—Laboratory Methods in Hematology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 6	IC	Lab, AV, EPP	64	2/16/59	3/12/59	C; 16 days	200
Medicine PM 22—Laboratory Methods in Blood Banks	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 6	II	Lab, PD, Lec, O, AV	24	3/31/59	5/ 5/59	I; 6 sessions 4 hr. weekly, Tuesdays	50

Key will be found on page 1954.

HEMATOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
5112-A. Hematology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, Lec, Pan, O, AV	35	11/10/58	11/14/58	C; 5 days	85
5424-A. Clinical Hematology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, LC, Lec, Pan, O	20	4/ 7/59	5/28/59	I; 16 sessions 1¼ hr. twice weekly, Tuesdays, Thursdays	50
Hematology	Albert Einstein Medical Center Northern Division York and Tabor Rds., Philadelphia 41	G Lim 20	II	PD, LC, BR, Sem, Pan, O, AV	30	2/13/59	4/24/59	I; 10 sessions 3 hr. weekly, Fridays	50
Hematology Conference	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 10	II	Sem, Lec, Pan, O, AV	16	9/58	12/58	I; Unknown	25
Clinical Hematology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 10	II	Lec, Pan, O, AV	Unknown	1/59	5/59	I; 16 sessions	25

INFERTILITY

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Infertility	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	PD, Sem, Lec, Pan, O, AV		Spring/59		Unknown	Unknown
464-A. Infertility	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 16	IC	Lab, PD, Clin C, Surg, Lec, O, EPP	21	12/ 1/58	12/ 3/58	C; 3 days	50

INTERNAL MEDICINE

(See also Allergy, Basic Sciences, Cardiovascular Disease, Clinical Pathology, Dermatology, Electrocardiography, Endoscopy, Ephebology, Gastroenterology, Hematology, Neurology, Occupational Medicine, Peripheral Vascular Disease, Physical Medicine and Rehabilitation, Psychiatry, Pulmonary Disease, Radiology, Radioisotopes)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Course In A Phase of Internal Medicine	California Medical Assoc. 2975 Wilshire Blvd., Los Angeles; course at University of California School of Medicine, San Francisco	S Lim 60	IC	PD, LC, Lec, Pan, O	12	2/23/59	2/25/59	C; 3 days	25
Management of Psychosomatic Symptoms in Internal Medicine	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	II	Sem, Lec, Pan, O, AV		Fall/58		Unknown	Unknown
Internal Medicine	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	II	Sem, Lec, Pan, O, AV		Fall/58		Unknown	Unknown
Teaching Clinics	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 75	II	PD, Sem, Lec, Pan, O, AV	24	9/25/58	12/18/58	I; 12 sessions 2 hr. weekly, Thursdays	50
Physiological and Clinical Aspects of Respiration	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	6	10/15/58	10/15/58	C; 1 day	20
Physiological and Clinical Aspects of the Kidney	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	6	11/19/58	11/19/58	C; 1 day	20
Arthritis and Rheumatism	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	PD, Sem, Lec, Pan, O, AV	6	Mar/59	Mar/59	C; 1 day	Unknown
855—Intensive Review of Internal Medicine	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S Lim 50	IC	Lec, AV	40	9/22/58	10/ 4/58	C; 10 days	65
852—Bedside Clinics in Internal Medicine	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G	II	PD, LC, BR, Lec, Pan	24	10/ 2/58	1/ 8/59	I; 12 sessions 2 hr. weekly, Thursdays	65
872—Workshops in Water and Electrolyte Balance	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G Lim 100	IC	PD, Sem, Surg, Pan	24	11/14/58	11/16/58	C; 3 days	75

8th Annual Symposium of San Diego County Heart Association	San Diego County Heart Association 1614 Fourth Ave., San Diego, Calif.; course at U. S. Naval Hospital, San Diego 34, Calif.	B	IO	PD, Lec, Pan, O, AV	6	10/31/58	10/31/58	O; 1 day	5
A Series of Postgraduate Medical Programs	U. S. Veterans Administration Hospital (Fort Miley) 42nd Ave., and Clement St., San Francisco	G Lim 300	II	Lab, PD, LC, Sem, Lec, Pan	12	4/59	5/59	I; 0 sessions 2 hr. weekly, Tuesdays	15 for Academy Members; 20 Non-members
Internal Medicine—Selective Review	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IO	PD, Lec, Pan, O, AV		9/13/58	9/17/58	C; 5 days	100
Postgraduate Course for Physicians	Contra Costa County Heart Association 2031 N. Main St., Walnut Creek, Calif.; course at Contra Costa County Hospital, Martinez, Calif.	G Lim 75	II	Lec, O.	16	2/ 2/59	4/ 6/59	I; 8 sessions 2 hr. weekly, Mondays	10
Pathophysiology of Fluid and Electrolyte Balance	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	II	Sem, Lec		9/58	12/58	I; 11 sessions 1½ hr. weekly	10
Problems in Cardio-Pulmonary Diseases	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	PD, Sem, Lec, Pan, O, TV	16	10/16/58	10/18/58	O; 3 days	35
Recent Advances in Internal Medicine	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B Lim 120	IO	Lec, Pan, O, AV	40	6/59	6/59	C; 5 days	Unknown
Present Concepts in Internal Medicine	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Letterman Army Hospital, San Francisco	G Lim 100	IC	Lab, LC, Sem, Lec, Pan, O, AV	35	10/27/58	10/31/58	C; 5 days	Nil
Seminar in Internal Medicine—Hematology and Gastrointestinal Disorders	University of Florida, College of Medicine Division of Postgraduate Education J. Hillis Miller Health Center Gainesville, Fla	B	IC	Lab, PD, Clin C, Sem, Lec, Pan, O, AV	15	3/59		C; 2½ days	25
Professor Pro Tempore in Medicine	Mt. Sinai Hospital of Greater Miami 4300 Alton Rd., Miami Beach 40, Fla	G Lim 150	IC	PD, LC, BR, Clin C, Lec, Pan, O	18	9/58	5 days later	C; 5 days	Nil
Seminar in Diabetes and Related Disorders	President, Florida Diabetes Association P. O. Box 187, Tallahassee, Fla.	B	IC	Clin C, Sem, Lec, Pan, O	12	10/58		O; 2 days	15
Internal Medicine for the Internist	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 50	IC	Sem, Lec, O	14	9/29/58 1/20/59	10/ 4/58	C; 6 days	125
Course II in Internal Medicine	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 30	IO	Lab, PD, LC, BR, Clin C, Lec, O, AV, EPP	80	10/20/58 5/11/59	11/ 1/58	C; 12 days	125
Fluid and Electrolyte Balance	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IO	Lec, Pan, O, AV	7	12/18/58	12/18/58	O; 1 day	10
Treatment of Hypertension	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IO	Lec, Pan, O, AV	7	1/30/59	1/30/59	O; 1 day	10
Internal Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IC	PD, LC, BR, Sem, Lec, Pan, O, AV, TV	28	11/10/58	11/13/58	O; 4 days	60
Emergencies in Medicine	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IO	Sem, Lec, Pan	28	1/28/59	1/31/59	C; 3½ days	25
Internal Medicine 2	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Boston City Hospital, Boston	S Lim 10	IO	Lab, PD, BR, Clin C, Lec		9/ 8/58	12/ 5/58	C; 65-70 days	400
Diabetes and Endocrinology in Relation to General Medicine	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at New England Deaconess Hospital, Boston 15	G Lim 35	IO	PD, LC, BR, Clin C, Sem, Lec, O, AV	21	10/ 6/58	10/ 8/58	O; 3 days	30
Recent Advances in Internal Medicine	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Peter Bent Brigham Hospital, Boston 15	S Lim 125	IO	Lab, PD, Clin C, Lec	38	6/ 1/59	6/ 6/59	C; 6 days	125
Internal Medicine 3	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston 14	G Lim 35	IO	PD, Clin C, Lec	180	6/15/59	7/25/59	C; 30 days	300
Review of Recent Advances in Internal Medicine	New England Center Hospital 171 Harrison Ave., Boston	S Lim 100	IC	PD, LC, Clin C, Sem, Lec, Pan, O	33	10/ 6/58	10/11/58	C; 5½ days	50
Clinical Internal Medicine	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 70	II	PD, Clin C, Lec, Pan, AV	67	10/ 3/58	2/20/59	I; 10 sessions 3½ hr. weekly, Thursdays	65
Recent Advances in Therapeutics	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IO	PD, Clin C, Lec, Pan, O, AV	35	3/23/59	3/27/59	C; 5 days	50

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INTERNAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Rheumatology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	30	4/20/59	4/24/59	C; 5 days	50
Metabolism and Endocrinology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	35	4/27/59	5/ 1/59	C; 5 days	50
Medical Seminars	Highland Park General Hospital 369 Glendale Ave., Highland Park, Mich.	G Lim 30	II	PD, LC, Clin C, Sem, Lec, Pan, O, AV	25	10/ 1/58	3/15/59	I; 1 hr. weekly, Wednesdays	Unknown
Internal Medicine for Internists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, O, AV	15	3/16/59	3/18/59	C; 3 days	40
Basic Concepts of Water and Electrolyte Balance	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	30	3/30/59	4/ 3/59	C; 5 days	65
Recent Advances in Internal Medicine	St. Michael's Hospital 306 High St., Newark, N. J.	G Lim 50	II	PD, LC, BR, Clin C, Lec, O, AV	20	9/58	2/59	I; 10 sessions 2 hr. weekly, Wednesdays	25
Clinical Pharmacology and Therapeutics	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Elizabeth Hospital, Elizabeth, N. J.	G Lim 50	II	Lec, O, AV	15	Unknown		I; 10 sessions 1½ hr. weekly, Wednesdays	50
Modern Concepts in Internal Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Elizabeth General Hospital, Elizabeth, N. J.	G Lim 50	II	Lec, O, AV	15	Unknown		I; 10 sessions 1½ hr. weekly	50
Modern Concepts in Internal Medicine	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Fitkin Memorial Hospital, Neptune, N. J.	G Lim 50	II	Lec, O, AV	15	9/30/58	12/ 2/58	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Recent Advances in Internal Medicine and Therapeutics	Middlesex General Hospital 180 Somerset St., New Brunswick, N. J.	G	II	Sem, Lec, O	72	9/17/58	6/24/59	I; 36 sessions 2 hr. weekly, Wednesdays	100 (interns and residents of outside hospitals 25)
Metabolic Aspects of Renal Disorders	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, AV	6	11/13/58	11/13/58	C; 1 day	12
Nutritional Metabolic Problems	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	12/ 4/58	12/ 4/58	C; 1 day	12
Acute and Chronic Pyelonephritis	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	1/15/59	1/15/59	C; 1 day	12
Recent Advances in Medicine	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	2/19/59	2/19/59	C; 1 day	12
Arthritis	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	10/ 1/58	10/ 2/58	C; 2 days	30
Recent Advances in Chest Diseases	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, LC, Sem, Lec, Pan, O, AV	14	10/22/58	10/23/58	C; 2 days	30
Disorders of the Liver—Part of course entitled "Application of Modern Medicine to Everyday Practice"	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Doctors Hospital Freeport, N. Y.	G Lim 30	II	Sem	9	10/28/58	12/ 2/58	I; 6 sessions 1½ hr. weekly, Tuesdays	18
Rheumatic Fever and Rheumatic Heart Disease	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G	II	Lec	6	10/31/58	11/21/58	I; 4 sessions 1½ hr. weekly, Fridays	10
Diabetes—Part of course entitled "Application of Modern Medicine to Everyday Practice"	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Doctors Hospital Freeport, N. Y.	G Lim 30	II	Sem	6	12/ 9/58	1/ 6/59	I; 4 sessions 1½ hr. weekly, Tuesdays	12
Physical Diagnosis and Recent Advances in Internal Medicine	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 5	II	BR, Clin C	20	2/19/59	4/23/59	I; 10 sessions 2 hr. weekly, Thursdays	20
Current Trends in Internal Medicine	Long Island Jewish Hospital 270-05 76th Ave., New Hyde Park, N. Y.	G Lim 40	II	PD, Lec	16	2/ 1/59	2/28/59	I; 8 sessions 2 hr. twice weekly, Tuesdays, Thursdays	25

[illegible] of Diabetes Mellitus and Its Complications	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Chronic Disease Hospital, Brooklyn, N. Y.	G Lim 30	II	PD, Lec	8	10/58	12/58	I; 8 sessions 1 hr. weekly, Thursdays	20
Recent Advances in Internal Medicine	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Kings County Hospital, Brooklyn, N. Y.	G Lim 40	II	Lec, O	15	10/58	12/58	I; 10 sessions 1½ hr. weekly, Wednesdays	30
Modern Therapeutics in Internal Medicine	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 30	II	Lec	15	4/59	6/59	I; 10 sessions 1½ hr. weekly, Thursdays	30
Diabetes and Basic Metabolic Problems	American Diabetes Association, Inc. One E. 45th St., New York 17; course at The Chase-Park Plaza Hotels St. Louis 8	G Lim 250	IO	Sem, Lec, Pan	20	1/21/59	1/23/59	C; 3 days	50 members; 100 nonmembers
Medicine PM 71—Internal Medicine	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, BR, Sem, Lec, EPP	76	9/23/58 2/ 3/59	1/27/59	I; 10 sessions 4 hr. weekly, Tuesdays	150
Medicine PM 80—Diseases of the Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Bellevue Hospital, New York	G Lim 6	IC	BR, Clin C, Lec, O, AV	140	10/ 1/58 2/ 2/59	10/31/58	C; 20 days	125
Medicine PM 50—Diseases of the Liver	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	PD, BR, Lec, O, AV	39	10/ 6/58	12/29/58	I; 13 sessions 3 hr. weekly, Mondays	100
Medicine PM 81—Arthritis	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Hospital for Joint Diseases New York 35	G	IC	Lab, LC, Lec, O, AV	16½	10/23/58 4/23/59	10/25/58	C; 3 days	100
Medicine PM 49—Office Management of Diseases of Metabolism	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IC	PD, Lec, Pan, O, AV	14	11/14/58	11/15/58	C; 2 days	50
Medicine PM 71—Diseases of the Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	Sem, Lec, O, AV	50	1/ 6/59	5/26/59	I; 20 sessions 2½ hr. weekly, Tuesdays	100
Arthritis	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	II	Lab, PD, LC, BR, Clin C, Lec, O	16	10/ 1/58 4/ 1/59	10/31/58	I; 8 sessions 2 hr. twice weekly, Tuesdays, Fridays	50
5139-A. Tutorial Course in Internal Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 1	PT	Lab, PD, Clin C, Lec, O		Arranged		Arranged	150 per mo.
512-A. Clinical Internal Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	18, 96 or 111	9/ 4/58 1/ 8/59 3/ 5/59	3, 6 or 9 mo. later	1 hr. weekly, Thursdays	60 for 3 mo.
518-A. Problems in Clinical Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	PD, LC, Clin C, Lec, O, AV, EPP	75	10/31/58	4/24/59	I; 25 sessions 3 hr. weekly, Fridays	75
5110-A. Arthritis and Allied Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 35	IC	PD, LC, BR, Lec, O, AV	35	11/10/58 6/ 8/59	11/14/58	C; 5 days	85
5111-A. Diabetes Mellitus, Hypertension and Hypoglycemia	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	IC	PD, Lec, Pan, O	21	11/10/58	11/12/58	C; 3 days	50
5119-A. Seminar in Internal Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	280	4/ 6/59	5/29/59	C; 40 days	250
5120-A. Treatment of Renal Failure and Hypertension	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 40	II	Sem, Lec	24	4/ 6/59	5/25/59	I; 8 sessions 3 hr. weekly, Mondays	35
5122-A. Acute and Chronic Diseases of the Chest	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	Clin C, Lec, Pan, O, AV	16	4/ 6/59	5/25/59	I; 8 sessions 2 hr. weekly, Mondays	40

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INTERNAL MEDICINE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
5423 A Arthritis and Allied Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave, New York 16	G Lim 35	II	PD, LC, BR, Lec, O, AV	24	4/ 7/59	5/26/59	I; 8 sessions 3 hr weekly, Tuesdays	55
5427 A Diseases of the Liver and Biliary Tract	New York University Post-Graduate Medical School 550 First Ave, New York 16	G Lim 15	II	PD, LC, Clin C, Lec, Pan, O	16	4/ 8/59	5/27/59	I; 8 sessions 2 hr weekly, Wednesdays	45
5431 A Problems in Diagnosis	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 20	II	PD, Lec, Pan, O, EPP	14	4/10/59	5/29/59	I, 8 sessions 1¾ hr weekly, Fridays	35
5435 A Symposium on Modern Therapeutics in Internal Medicine	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	70	6/ 8/59	6/19/59	C, 10 days	100
5437-A The Management of Chronic Kidney Disease	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 30	IC	Clin C, Lec, Pan, O	14	6/22/59	6/23/59	C; 2 days	35
5438-A The Management of Hypertension	New York University Post Graduate Medical School 550 First Ave, New York 16	G	IC	Lab, Lec, O	14	6/24/59	6/25/59	C; 2 days	35
New Therapeutics	Rochester General Hospital 501 W Main St, Rochester, N Y	G	IC	Lec, Pan, AV	6	3/26/59	3/26/59	C, 1 day	5
Internal Medicine	State University of New York Upstate Medical Center 766 Irving Ave, Syracuse, N Y	G	II	Sem, Lec, O, AV	21	4/ 9/59	5/21/59	I; 7 sessions 3 hr. weekly, Thursdays	15
A Review of Diabetes and Metabolic Diseases	Duke University School of Medicine Durham, N C	G	IC	Lab, PD, LC, BR, Sem, Lec	Unknown	3/59			Unknown
North Dakota Academy of General Practice Refresher Course—Recent Concepts of Cardiovascular and Liver Diseases	University of North Dakota School of Medicine Grand Forks, N D	G	IC	Lec, Pan	10	11/21/58	11/22/58	C; 2 days	Unknown
Selected Topics in Internal Medicine	Registrar, School of Medicine, Western Reserve University 2109 Adelbert Rd, Cleveland; course at University Hospitals of Cleveland, Cleveland	S Lim 80	II	PD, Clin C, Lec, Pan, O, AV	24	3/ 4/59	4/22/59	I; 8 sessions 3 hr weekly, Wednesdays	30
Sessions in Rheumatic Diseases	Ohio State University College of Medicine 11th and Neil Aves, Columbus 10, Ohio	G	IC	PD, LC, Clin C, Lec, Pan	8	10/18/58	10/19/58	C, 2 days	Nil
Metabolic Disorders	Dr Gaston B Hannah Southwestern Ohio Society of General Physicians Sharon and Willow Ave, Glendale, O; course at Hartwell Country Club, Cincinnati	G	IC	Sem, Lec, Pan, O, AV	5	1/18/59	1/18/59	C, 1 day	10
Advance in Arthritis and Related Disorders—2nd Oklahoma Colloquy	University of Oklahoma Medical Center 801 N E 13th St, Oklahoma City	S Lim 300	IC	PD, LC, Clin C, Lec, Pan, O, AV	21	11/12/58	11/15/58	C; 4 days	25 for entire course; 10 per day
Fifth Annual Surgery, Radiology, Pathology Symposium	University of Oklahoma Medical Center 801 N E 13th St, Oklahoma City	S	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	12	5/ 8/59	5/ 9/59	C; 2 days	20
The Physiological Basis of Internal Medicine	American College of Physicians 4200 Pine St, Philadelphia 4, course at Duke University School of Medicine, Durham, N C	S Lim 90	IC	Lec, O, AV	35	10/13/58	10/17/58	C, 5 days	Unknown
Physiological Basis of Internal Medicine	American College of Physicians 4200 Pine St, Philadelphia 4, course at Duke University School of Medicine, Durham, N C	S	IC	Lec, Pan, O, AV	35 40	10/13/58	10/17/58	C, 5 days	30 A C P members; 60 nonmembers
Recent Advances in Internal Medicine	American College of Physicians 4200 Pine St, Philadelphia 4, course at University of Colorado School of Medicine, Denver	S	IC	Clin C, Lec, Pan, O, AV	35 40	6/15/59	6/19/59	C, 5 days	30 A C P members; 60 nonmembers
Recent Developments in Internal Medicine	American College of Physicians 4200 Pine St, Philadelphia 4, course at University of Cincinnati College of Medicine, Cincinnati	S	IC	Clin C, Lec, Pan, O, AV	35 40	6/59		C, 5 days	30 A C P members,

Renal Disease	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 8	II	Lec, AV	16	9/58	1/59	I; Unknown	25
Metabolic Diseases	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G	II	Lec	10	10/58	12/58	I; 10 sessions 1 hr. weekly	25
Diseases of the Chest	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 5	II	Sem, Lec, O, AV	15	10/ 6/58	1/26/59	I; 15 sessions 1 hr. weekly, Mondays	30
Rheumatic Diseases and Allied Conditions	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 10	II	Lec, Pan, AV	Unknown	1/19/59	5/59	I; Unknown	45
A Postgraduate Review in Medicine	Vanderbilt University School of Medicine 21st Ave. South, Nashville, Tenn.	G	IC	PD, LC, Clin C, Lec, Pan, O	6	Spring/59	Spring/59	C; 1 day	15
Fluid and Electrolyte Balance	University of Washington School of Medicine Seattle 5	G Lim 10	IC	Lab, PD, Sem, Lec, O, EPP	22½	9/24/58	9/27/58	C; 3½ days	45
Changing Attitudes in Coronary Heart Disease and Disorders of the Heart and Lungs	University of Washington School of Medicine Seattle 5	G Lim 500	IC	Sem, Lec, O	9	10/17/58	10/18/58	C; 2 days	Unknown
Hematology and Hypertension	Assistant to the Dean University of Wisconsin Medical School 418 N. Randall Ave., Madison 6, Wis.	S Lim 100	IC	PD, Lec, Pan, O, AV	18	4/ 9/59	4/11/59	C; 2½ days	30

MALIGNANT DISEASE

(See also Gynecology, Pathology)

Rocky Mountain Cancer Conference	Colorado State Medical Society 835 Republic Bldg., Denver 2; course at Shirley Savoy Hotel, Denver	G	IC	Lec, Pan	Unknown	7/ 9/59	7/10/59	C; 2 days	Nil
Cancer Cytology	The Cancer Institute at Miami 1155 Northwest 14th St., Miami, Fla	G	IC or PT	Lab, PD, Sem, Lec, Pan, O, AV, EPP		any time		Arranged	150 1 mo. 350 6 mo. 650 12 mo.
Cancer Seminar	Florida State Board of Health 1217 Pearl St., Jacksonville, Fla ; course at Tampa Hotel, Tampa, Fla	G	IC	Sem	15	11/19/58	11/21/58	C; 3 days	Nil
Symposium on Malignancy	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	Lec, Pan, O, AV	8	3/31/59	4/ 1/59	C; 2 days	Nil
Cancer Seminar	University of Mississippi Medical Center, Secretary, Postgraduate Education Committee 2500 N. State St., Jackson, Miss.	G Lim 150	IC	PD, Clin C, Sem, Lec, Pan, O, AV	7	12/ 4/58	12/ 4/58	C; 1 day	Nil
Medicine PM 72-Neoplastic Diseases	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, Sem, Lec, O, AV	76	9/ 9/58 1/27/59	1/20/59	I; 18 sessions 4 hr. weekly, Tuesdays	150
Diagnosis and Management of Early Cancer	Memorial Center for Cancer and Allied Diseases 444 E. 68th St., New York 21	G Lim 20	IC	PD, LC, Sem, Lec, Pan, O, AV, EPP	24	9/29/58	10/ 1/58	C; 3 days	40
Malignant Disease	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	B	II	PD, LC, Lec, Pan, O, AV	21	Spring/59		Unknown	15
Status of Cancer Chemotherapy	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B Lim 270	IC	PD, Lec, Pan	10	11/14/58	11/15/58	C; 2 days	5
13th Annual Symposium on Fundamental Cancer Research	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B Lim 270	IC	Lec, Pan	15	3/ 5/59	3/ 7/59	C; 3 days	5

NEUROLOGY

(See also Anatomy, Basic Sciences, Electroencephalography, Neurology and Psychiatry, Pathology, Pediatrics, Surgery)

Physiological and Clinical Aspects of the Nervous System	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	6	1/11/59	1/11/59	C; 1 day	20
Clinical Neurology	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	Lec, Pan, O, AV	14	1/59		C; 2 days	40
10th Western Institute on Epilepsy	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B	IC	Lec, Pan, O, AV	16	10/30/58	11/ 1/58	C; 3 days	35

Key will be found on page 1954.

NEUROLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Clinical Neurology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S Lim 40 to 50	II	Lec, O	22	9/22/58	12/ 1/58	I; 22 sessions 1 hr. weekly, Mondays	Nil
Pediatric Neurology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S Lim 60	II	Lec, O	6	12/ 1/58	12/ 8/58	I; 6 sessions 1 hr. weekly, Mondays	Nil
The Neuromuscular Diseases of Children With Special Emphasis on Cerebral Palsy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 30	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	80	7/ 6/59	7/17/59	C; 11 days	250
Neurology Conference	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IC	PD, LC, Lec, Pan, O, AV, EPP	6	3/19/59	3/19/59	C; 1 day	15
Neurological Medicine	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Boston City Hospital, Boston	S Lim 20	IC	Lab, PD, Lec	38	6/ 1/59	6/ 6/59	C; 6 days	100
Neurology	New England Center Hospital 171 Harrison Ave., Boston	S Lim 50	IC	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	20	4/29/59	5/ 2/59	C; 4 days	Unknown
Lecture Course in Neurology	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 25	II	Lec	6	10/ 1/58	11/ 5/58	I; 6 sessions 1 hr. weekly, Wednesdays	15
Neurology PM 61—Advanced Neurology	Assistant Dean for Postgraduate Medical Education Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	IC	PD, LC, Sem, O, AV, EPP	420	Arranged every 3 mo.		3 mo. 5 days weekly, may be extended in 3 mo. units	150
Cerebral Palsy PM 1	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G	IC	LC, Lec, Pan, O, AV	105	10/13/58 3/ 2/59	10/31/58	C; 15 days	100
Neurology PM 60-Review of Neurology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	Lab, PD, Lec, O, AV	48	11/ 3/58	11/29/58	I; 16 sessions 3 hr. 4 times wk., Mondays, Wednesdays, Fridays, Saturdays	150
Neurology PM 30-Clinical Neurology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IC	PD, Sem, Lec, O, AV	30	3/30/59	4/ 3/59	C; 5 days	75
557-A. Seminar on Epilepsy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	II	Lec, O, AV	6	9/ 3/58	10/ 8/58	I; 6 sessions 1 hr. weekly, Wednesdays	35
Review of Neurology	Inquire of: Dr. Geoffrey Osler 11 E. 68th St., New York 21; course at Goldwater Memorial Hospital and Manhattan State Hospital, New York	S Lim 24	II	Lab, PD, LC, Lec, AV	100	9/17/58	12/10/58	I; 40 sessions 2½ hr. 5 days a week, Mondays, Tuesdays, Wednesdays, Fridays, Sundays	175

NEUROLOGY AND PSYCHIATRY

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Psychiatry PM 1	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	IC	Lab, PD, Lec, O, AV	400	10/ 6/58	12/12/58	C; 50 days	300
647-A. Neurology and Psychiatry	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	IC	PD, LC, Lec	420	9/15/58	12/ 5/58	C; 12 wk.	300
710 Basic Psychiatry and Neurology	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S	II	LC, Lec	24	10/ 3/58	[illegible]	I; 16 sessions	[illegible]

Refresher Course in Neuropsychiatry	Ohio State University College of Medicine 11th and Neil Aves., Columbus 10, Ohio; course at Columbus *Psychiatric* Institute and Hospital, Columbus, Ohio	S Lim 10	IC	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	80	11/ 3/58	11/28/58	C; 20 days	Nil
Neurology-Psychiatry Lectures	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G	II	Lec	30	9/58	5/59	I; 30 sessions 1 hr. weekly, Tuesdays	50

OBSTETRICS

(See also Infertility)

Postgraduate Obstetric-Pediatric Seminar	Florida State Board of Health—Bureau of Maternal and Child Health P. O. Box 210, Jacksonville 1, Fla.; course at Daytona Plaza Hotel, Daytona Beach, Fla.	G Lim 425	IC	Sem, Lec, Pan, O, AV	15	9/ 8/58	9/10/58	C; 3 days	Nil
Course I in Obstetrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 14	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	75	9/22/58 10/27/58 2/23/59 3/30/59 5/ 1/59	10/ 4/58	C; 12 days	150
Obstetrics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, LC, Lec, Pan, O, AV	18	11/ 3/58	11/ 5/58	C; 3 days	40
Clinical Obstetrics	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Boston Lying-in Hospital, Boston	G Lim 6	IC	PD, LC, BR, Clin C	120-130	10/ 1/58 11/ 1/58 4/ 1/59 5/ 1/59	10/31/58	C; 27 days	150
Obstetrics for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, O, AV	15	10/ 6/58	10/ 8/58	C; 3 days	40
Obstetrics	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha; course at Lincoln General Hospital, Lincoln, Neb	G	IC	Clin C, Sem, Lec, Pan, O, AV	6	3/26/59	3/26/59	C; 1 day	10
Seventh Annual Spring Postgraduate Assembly	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	Sem, Lec, Pan, O, AV	18	4/16/59	4/17/59	C; 3 days	30
Modern Concepts in Obstetrics	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Mary's Hospital, Passaic, N. J.	G Lim 50	II	Lec, O, AV	18	Unknown		I; 12 sessions 1½ hr. weekly	50
Obstetrics—65 OM	Department of Postgraduate Medical Education, Seton *Hall College* of Medicine and Dentistry, 31 Clinton St., Newark 2, N. J.; course at Margaret Hague Hospital, Jersey City, N. J.	G	PT	Lab, PD, LC, BR, Clin C, Lec, EPP		Arranged	3 months later	90 days	350
Obstetrics—66 OM	Department of Postgraduate Medical Education, Seton Hall College of Medicine and Dentistry, 31 Clinton St., Newark 2, N. J.; course at Margaret Hague Hospital, Jersey City, N. J.	G	PT	Lab, PD, BR, Clin C, Lec, EPP		Arranged	1 month later	30 days	100
Obstetrics P.M. 80	Department of Postgraduate Medical Education Seton Hall College of Medicine and Dentistry 31 Clinton St., Newark 2, N. J.; course at Margaret Hague Maternity Hospital, Jersey City, N. J.	G	II	Lab, LC, BR, Clin C, Lec, EPP	30	Arranged	3 mo. later	I; 1 day each wk.	350
Modern Concepts in Obstetrics	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Mercer Hospital, Trenton, N. J.	G Lim 50	II	Lec, O, AV	18	1/59		I; 12 sessions 1½ hr. weekly	50
Obstetrics	University of Buffalo School of Medicine 3435 Main St., Buffalo	G Lim 16	IC	PD, Sem, Lec, O, AV	14	3/11/59	3/12/59	C; 2 days	30
eps Course (Manikin)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	II	PD, LC, BR, Clin C, Lec, O, AV	21	10/ 1/58 4/ 1/59	11/12/58	I; 12 sessions 2 hr. twice a week, Wednesdays, Fridays	150
rics	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	G Lim 2	IC	PD, LC, BR, Sem, Lec, O, AV	40	Arranged	Arranged	C; 5 days	25

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OBSTETRICS AND GYNECOLOGY

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Obstetrics and Gynecology Traineeship	University of Arkansas Medical School Department of Obstetrics and Gynecology 4301 W. Markham, Little Rock, Ark	G Lim 3	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, AV, TV, EPP		Arranged		Arranged	Unknown
Obstetrics and Gynecology	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	PD, Sem, Lec, Pan, O, AV	12	11/14/58	11/15/58	C; 2 days	50
Obstetrics and Gynecology	University of California Medical Center Second and Parnassus Ave, San Francisco	G Lim 100	IC	Lec, Pan, O, AV	21	9/18/58	9/20/58	C; 3 days	50
Obstetrics and Gynecology	University of Colorado School of Medicine 4200 E Ninth Ave, Denver 20	S Lim 50	IC	Sem, Lec, Pan, O, AV	6	6/59	6/59	C; 3 days	30
Obstetrics and Gynecology	Indiana University School of Medicine 1100 W. Michigan St, Indianapolis 7	G	IC	Lec, Pan, O, AV	12	3/ 4/59	3/ 5/59	C; 2 days	20
Obstetrics and Gynecology	State University of Iowa College of Medicine University Hospitals, Iowa City	B	IC	PD, BR, Lec, Pan, O, AV	6	1/14/59	1/14/59	C; 1 day	15
Pathology of Obstetrics and Gynecology	Harvard Medical School, Courses for Graduates 25 Shattuck St, Boston 15; course at Free Hospital For Women, Brookline, Mass	S Lim 12	II	Lab, Lec	144	1/ 8/59	5/21/59	I; 20 sessions 7 hr. weekly, Thursdays	150
Obstetrics and Gynecology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	18	1/28/59	1/30/59	C; 3 days	30
Obstetrics and Gynecology	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha 5	G	IC	Clin C, Sem, Lec, Pan, O, AV	12	1/15/59	1/16/59	C; 2 days	20
In Hospital Review In Obstetrics and Gynecology	University of Nebraska College of Medicine 42nd and Dewey, Omaha 5	G Lim 5	PT	PD, LC, BR, Clin C, Sem, Surg, O, AV, EPP	40	Spring/59		5½ days	50
Recent Advances in Obstetrics and Gynecology	Albany Medical College 47 New Scotland Ave, Albany 8, N Y	G	II	PD, LC, Clin C, Sem, O, AV	16	2/26/59	3/19/59	I; 4 sessions 4 hr. weekly, Thursdays	20
Gynecology and Obstetrics Including Manikin Obstetrics and Operative Gynecology (Cadaver)	New York Polyclinic Hospital 345 W 50th St, New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	400	10/ 1/58 4/ 1/59	11/30/58	C; 56 days	250
5610 A X Ray Diagnosis in Obstetrics and Gynecology	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 10	IC	PD, Lec, O, AV	35	10/20/58	10/24/58	C; 5 days	85
Obstetrical Gynecological Symposium	University of Oklahoma Medical Center 801 N E 13th St, Oklahoma City	B	IC	PD, Sem, Lec, Pan, O, AV	8	3/ 7/59	3/ 7/59	C; 1 day	5
Obstetrics and Gynecology Postgraduate Course	Hahnemann Hospital and Medical College 235 N Broad St, Philadelphia	G Lim 30	II	Lab, PD, Clin C, Pan, O, AV	24	9/24/58	12/10/58	I; 12 sessions 2 hr. weekly, Wednesdays	50
A Postgraduate Review in Obstetrics Gynecology	Vanderbilt University School of Medicine 21st Ave. South, Nashville, Tenn	G	IC	PD, LC, Clin C, Lec, Pan, O	6	Winter/ 1958-59	Winter/ 1958-59	C; 1 day	15
General Review of Obstetrics and Gynecology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25 Tex; course at University of Texas M D Anderson Hospital, Houston, Tex	G	II	Lec, Pan, AV	9	12/ 2/58	12/16/58	I; 3 sessions 3 hr. weekly, Tuesdays	20

OCCUPATIONAL MEDICINE

(See also General Practice, Radiology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Aviation Medicine	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV	18	10/22/58	10/24/58	C; 3 days	75
Multidisciplinary Approach to the Problems of Athletic Injuries	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Lec, Pan, O, AV	12	12/19/58	12/20/58	C; 2 days	10
The Prevention and Management of Athletic Injuries	University of Colorado School of Medicine 4200 E Ninth Ave, Denver 20	B	IC	PD, Lec, Pan, O, AV	24	8/59	8/59	C; 3 days	35
Clinical Physical Medicine and Athletic Injuries	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IC	PD, LC, BR, Lec, Pan, O, AV	9	11/21/58	11/22/58	C; 2 days	20
Clinical Traineeship in Public Health and Preventive Medicine	University of Kansas Medical Center 39th and Rainbow Blvd, Kansas City, Ks	G Lim 2	PT	PD, LC, BR, Clin C, Sem, Lec, O, AV	Varies	Arranged		Arranged	50 per mo in state; 100 per mo out of state

School Health	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	Sem, Lec, Pan, O, AV	7	10/ 9/58	10/ 9/58	C; 1 day	Nil
Extension Course in Public Health Qualifying for Grade II Local Health Officer in New York State	Albany Medical College 17 New Scotland Ave., Albany 8, N. Y.	G	II and HS	Sem, Lec, O, HS	30	any time	1 yr. later	Combination HS and 1 one day sessions for 6 days	25
Occupational Medicine 207—Public Health Aspects of Radiation	Columbia University School of Public Health and Administrative Medicine 600 W. 168th St., New York 32	G	II	Lec, O, AV		Arranged		Arranged	30
Occupational Medicine 202—Occupational Diseases	Columbia University School of Public Health and Administrative Medicine 600 W. 168th St., New York 32	G	II	Lec, O, AV	21	2/ 2/59	3/28/59	I; 8 sessions 3 hr. weekly, day to be arranged	30
Institute for Physicians in Industry	School of Public Health and Administrative Medicine, Columbia University 600 W. 168th St., New York 32	S	IC	Sem, Lec, Pan, O	36	2/ 6/59	2/10/59	C; 5 days	108
Occupational Medicine 203—Industrial Medical Organization	Columbia University School of Public Health and Administrative Medicine 600 W. 168th St., New York 32	G	II	Lec, O, AV	13½	3/30/59	5/28/59	I; 9 sessions 1½ hr. weekly, day to be arranged	30
Bureau of School Health Pre-Service Training Course	Dr. Robert S. Culbert, Director Department of Health 125 Worth St., New York 14; course at Kips Bay Health Center, New York	G Lim 10	IC	LC, Sem, EPP	90	9/58 3/59 5/59	Approximately 6 wk. later	C; 30 days	Nil
1811-A. Special Topics in Industrial Hygiene Laboratory Methods	New York University Post-Graduate Medical School 550 First Ave., New York 16	B	IC or II	Lab		Arranged		Arranged	Arranged
482-A. Industrial Hygiene	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 30	II	Lab, Lec		9/58	15 wk. later		90
189-A. Chemical Methods in Industrial Hygiene	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 10	II	Lab, Lec, AV		9/58	15 wk. later		100
188-A. Occupational Medicine for Physicians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	Sem, Lec, Pan, AV	280	9/15/58	11/ 7/58	C; 40 days	350 plus 25 for Field Trip
Occupational Health for Physicians	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 50	II	PD, Clin C, Sem, Lec, AV	90	9/18/58	5/14/59	I; 30 sessions 3 hr. weekly, Thursdays	300
184-A. Medical Aspects of Compensation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 100	IC	Sem, Lec, Pan, AV	35	10/20/58	10/24/58	C; 5 days	45
1813-A. Radiochemical Analysis	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	IC	Lab, Lec, AV	70	11/10/58	11/21/58	C; 10 days	90
186-A. Air Pollution	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 30	IC	Lab, Lec, AV, EPP	70	12/ 1/58	12/12/58	C; 10 days	90
180-A. Introduction to Radiological Health	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 35	IC	Lab, Lec, AV	70	1/ 5/59	1/16/59	C; 10 days	90
180 B. Radiological Health Laboratory	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 10	IC	Lab, Lec, AV	70	1/19/59	1/30/59	C; 10 days	90
182-B. Industrial Hygiene Laboratory	New York University Post-Graduate Medical School 550 First Ave., New York 16	G and non-Physicians Lim 10	II	Lab, Lec, AV		2/59	15 wk. later		90
1810 A. Industrial Toxicology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	Lab, Lec, AV		2/59	15 wk. later		100
1812 A. Radiation Hygiene Measurements	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	IC	Lab, Lec, AV	140	5/ 4/59	5/29/59	C; 20 days	180
School Health	State University of New York Upstate Medical Center 700 Irving Ave., Syracuse, N. Y.	G	IC	PD, Lec, O, AV	5	9/11/58	9/11/58	C; 1 day	10
Postgraduate Course in Aviation Medicine	Ohio State University Health Center, Columbus, Ohio	G Lim 40	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	36	9/ 8/58	9/12/58	C; 5 days	75
Treatment of Athletic Injuries	University of Oklahoma Medical Center 801 N.E. 13th St., Oklahoma City	G	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	12	4/10/59	4/11/59	C; 2 days	10

Key will be found on page 1974.

OPHTHALMOLOGY

(See also Ophthalmology and Otolaryngology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Postgraduate Conference in Ophthalmology	Stanford University School of Medicine 2398 Sacramento St., San Francisco	S Lim 30	IC	Lab, PD, Sem, Lec, Pan, O	29	Spring 1959		C; 5 days	100
Postgraduate Course on External Eye Diseases	University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 100	IC	PD, Clin C, Lec, Pan, AV	30	12/ 3/58	12/ 6/58	C; 4 days	65
Clinical Ophthalmology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Surg, O	50	Arranged By appointment	2 wk. later	10 days	50
Extraocular Muscles II—Diagnosis and Treatment of Strabismus	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 5	II	PD, LC, BR, Sem, Lec	200	Arranged		I; 100 sessions 2 hr., arranged	150
Extraocular Muscles I—Diagnosis and Treatment of Strabismus	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 5	IC	PD, LC, Sem, Lec	24	9/ 8/58	9/19/58	C; 10 days	100
Clinical Traineeship in Ophthalmology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP		Arranged	1 mo. later	30 days	50 in state; 100 out of state
Glaucoma	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S Lim 10	IC	PD, BR, Clin C, Lec, Pan, O, AV	14	12/12/58	12/13/58	C; 2 days	50
Ophthalmology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	PD, Clin C, Lec, Pan, O, AV	17	4/ 8/59	4/10/59	C; 3 days	40
Ophthalmology—Infectious Diseases of the Eye	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	S Lim 50	IC	Lab, Clin C, Sem, Lec	44	1/12/59	1/17/59	C; 5½ days	50
Lancaster Courses in Ophthalmology, Basic Science	Parker Heath, M.D., Director Ophthalmological Study Council Sullivan Harbor, Me.; course at Colby College, Waterville, Me.	B Lim 80	IC	Lab, Clin C, Sem, Lec, Pan, O, EPP	445	6/21/59	9/ 6/59	C; 11 wk.	325
Ophthalmology	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course also at Massachusetts Eye and Ear Infirmary, Boston	S Lim 30	IC	Lab, PD, Clin C, Lec	35-40 hr. wk.	9/22/58	3/11/59	C; 25 wk.	600
Ophthalmology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	S Lim 150	IC	Clin C, Lec, Pan, O	18	4/20/59	4/22/59	C; 3 days	50
Home Study Course in Ophthalmology	American Academy of Ophthalmology and Otolaryngology 15 Second St., S.W., Rochester, Minn.	S	HS(R)	Assigned reading		9/ 1/58	6/30/59	9 mo.	20
Seminar on Glaucoma	Brooklyn Eye and Ear Hospital 29 Green Ave., Brooklyn, N. Y.	S Lim 6	IC	PD, LC, Clin C, Lec, O, EPP	18	11/17/58 5/59	11/19/58	C; 3 days	50
External Eye Diseases and Ophthalmoscopy	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Chronic Disease Hospital, Brooklyn, N. Y.	G Lim 10	II	PD, Lec, AV	16	4/59	5/59	I; 8 sessions 2 hr. weekly, Wednesdays	30
Ophthalmology PM 31-Glaucoma	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 10	II	PD, Lec, O, AV, EPP	9	10/ 7/58	10/23/58	I; 6 sessions 1½ hr. twice weekly, Tuesdays, Thursdays	50
Ophthalmology PM 62-Glaucoma	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	S	II	PD, Sem, O, AV	16	10/20/58	12/ 8/58	I; 8 sessions 2 hr. weekly, Mondays	30
Ophthalmology PM 32-Ophthalmoscopy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 12	II	Lab, PD, Clin C, EPP	12	11/ 6/58	12/ 4/58	I; 8 sessions 1½ hr. twice weekly, Tuesdays, Thursdays	75
Ophthalmology PM 60-Elementary Ophthalmoscopy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G	II	PD, Lec, O, AV, EPP	18	1/ 7/59	3/ 5/59	I; 9 sessions 2 hr. weekly, Wednesdays	30
Ophthalmology PM 33-The Use of Schepens' Ophthalmoscope	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 8	II	Lab, PD, Sem, EPP	12	3/10/59	3/26/59	I; 6 sessions 2 hr. twice weekly, Tuesdays, Thursdays	50

Ophthalmology PM 30-Histopathology of the Eye	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 10	II	PD, Lec, O, AV, EPP	16	4/ 1/59	4/24/59	I; 8 sessions 2 hr. twice weekly, Wednesdays, Fridays	100
Plastic Eye Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 10	II	PD, LC, Surg, Lec, O, AV	12	11/ 3/58	11/20/58	I; 6 sessions 7 hr. Mondays, Thursdays, 3 wk.	200
Anomalies of Extraocular Muscles Including Ptosis	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 10	II	PD, LC, Surg, Lec, O, AV	20	11/ 4/58	11/ 8/58	I; 4 sessions 3 hr. on Tuesday, Wednesday, all day Friday, Saturday	100
Keratectomies and Keratoplasties	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 30	IC	Surg, Lec, O, AV, TV, EPP	11	11/ 4/58	11/ 5/58	C; 2 days	75
Gonioscopy and Tonography	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 15	IC	PD, Lec, O, AV, EPP	3	11/10/58 12/ 1/58	11/10/58	C; 1 day	15
Cataracts	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 12	IC	Lab, PD, Surg, Lec, O, AV, EPP	11	11/11/58	11/12/58	C; 2 days	75
Retinal Detachment	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 30	IC	PD, Surg, Lec, O, AV, EPP	14	11/14/58	11/15/58	C; 2 days	75
Pathology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 20	IC	Lec, O, AV	21	11/18/58	11/21/58	C; 3 days	100
Ocular Trauma	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	IC	PD, Lec, Pan, O, AV	22	11/24/58	11/26/58	C; 3 days	100
Biomicroscopy, Near Ultra-Violet Biomicroscopy, Gonioscopy and Tonography	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 20	IC	PD, Lec, O, AV, EPP	14	11/28/58	11/29/58	C; 2 days	75
Biomicroscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 8	II	PD, Lec, O, AV, EPP	16	12/ 1/58	12/24/58	I; 8 sessions 2 hr. twice weekly, Mondays, Wednesdays	80
Complications of Ophthalmic Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 25	II	Lab, Lec	10	12/ 1/58	12/31/58	I; 10 sessions 1 hr. twice weekly, Mondays, Wednesdays	50
Near Ultra-Violet Biomicroscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 12	II	PD, Lec, O, EPP	3	12/ 1/58	12/ 5/58	I; 3 sessions one hr. Monday, Wednesday, Friday	15
Ocular Photography	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 12	II	Lec, O, AV, EPP	8	12/ 1/58	12/ 5/58	I; 3 sessions 2 hr. thrice in one wk., Monday, Thursday, Friday	40
Clinical Bacteriology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 6 for lab. sessions	IC	Lab, Lec, O, AV, EPP	5	12/ 2/58	12/ 3/58	C; 2 days	25
Glaucoma	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 8	II	PD, Surg, Lec, O, AV	15	12/ 2/58	12/18/58	I; 6 sessions 2½ hr. twice weekly, Tuesdays, Thursdays	75
Ophthalmoscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 6	II	PD, Lec, O, AV, EPP	12	12/ 2/58	12/18/58	I; 6 sessions 2 hr. twice weekly, Tuesdays, Thursdays	60
Refraction	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 25	II	PD, Lec, O, AV	12	12/ 2/58	12/18/58	I; 6 sessions 2 hr. twice weekly, Tuesdays, Thursdays	60

Key will be found on page 1954.

OPHTHALMOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Ocular Allergy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	II	PD, Lec, O, AV	4	12/ 5/58	12/12/58	I; 2 sessions 2 hr. weekly, Fridays	20
Ocular Radiology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 9	IC	PD, Lec, O, AV	6	12/ 8/58	12/13/58	C; 1 hr. daily for 6 days	30
Pleoptics and Macular Function Testing	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 10	II	PD, Lec, O, AV, EPP	3	12/ 8/58	12/12/58	I; 3 sessions 1 hr. thrice one wk., Monday, Wednesday, Friday	15
Psychosomatic Factors in Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	II	Lec, O, AV	4	12/ 8/58	12/10/58	I; 2 hr. twice one wk., Monday, Wednesday	20
Ocular Neuro-Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	II	PD, Lec, O, AV	10	12/ 9/58	12/18/58	I; 5 sessions 2 hr. twice weekly, Tuesdays, Thursdays	50
Perimetry	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	II	Lec, O, AV	3	12/10/58	12/17/58	I; 2 sessions 1½ hr. Wednesdays two wk.	15
Aniseikonia	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	IC	Lec, O, AV	2	12/15/58	12/15/58	C; 1 day	10
Lacrimal Sac Surgery	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S	II	PD, Surg, Lec, O, AV	8	12/15/58	12/23/58	I; 4 sessions 2 hr Mondays, Tuesdays, two wk.	40
Medical Ophthalmoscopy	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 10	II	PD, Lec, O, EPP	6	12/15/58	12/19/58	I; 2 hr. Mondays, Wednesdays, Fridays, one wk.	30
Electrophysiology of the Eye	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 10	IC	Lab, PD, Lec, O, AV, EPP	6	12/29/58	12/31/58	C; 3 days	30
Ocular Biochemistry	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 8	IC	Lab, Lec, O, AV	7½	1/ 5/59	1/ 9/59	C; 5 days	35
Ocular Microbiology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 8	IC	Lab, Lec, O, AV, EPP	6	1/ 5/59	1/ 8/59	C; 4 days	30
Radioisotopes in Ophthalmology	Institute of Ophthalmology of the Americas New York Eye and Ear Infirmary 218 Second Ave., New York	S Lim 12	IC	Lab, PD, Lec, O, AV, EPP	15	1/ 5/59	1/ 9/59	C; 5 days	75
Ophthalmology with Operative Ophthalmology (Cadaver)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	360	10/ 1/58 4/ 1/59	12/31/58	C; 72 days	300
Refraction	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	PD, LC, Clin C, Lec	72	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	100
Ophthalmic Plastic Surgery	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 15	IC	PD, Surg, Lec, Pan, O, AV	15	11/17/58 3/16/59	11/21/58	C; 5 days	85
572-A. Surgery of the Cornea	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 40	IC	Lab, PD, LC, Surg, Lec, O, AV, TV, EPP	35	12/ 1/58	12/ 5/58	C; 5 days	225
573-A. Neuro-Ophthalmology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim	IC	PD, Lec, O, AV	15	1/19/59	1/23/59	C; 5 days	55
574-A. Annual Review of Ophthalmological Advances	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	PD, Lec, Pan, O, AV	15	2/12/59	2/14/59	C; 2½ days	100
Motor Anomalies of the Eye (Part I)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 25	IC	PD, Clin C, Lec, Pan, O, AV	42	3/ 2/59	3/ 7/59	C; 6 days	100
576-A. Motor Anomalies of the Eye (Part II)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 26	IC	PD, LC, Clin C, Lec, Pan, O, AV, EPP	35	3/ 9/59	3/13/59	C; 5 days	85
577-A. Ocular Expressions of Systemic Disease	New York University Post-Graduate				15	3/16/59	3/20/59	C; 5 days	55

578-A. Surgery of the Eye	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 11	IO	Lab, PD, Surg, Lec, Pan, O, AV	42	3/30/59	4/ 4/59	C; 6 days	125
5710 A. Histopathology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim	IO	Lab, Lec, O, AV	15	5/ 4/59	5/ 8/59	C; 5 days	100
579 A. Ophthalmoscopy	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim	IO	PD, Lec, O, AV	15	5/ 4/59	5/ 8/59	C; 5 days	55
Ophthalmology	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.; course at Hotel Syracuse, Syracuse	S Lim 40	IC	Lec, Pan, AV	14	12/ 5/58	12/ 6/58	C; 2 days	25
Postgraduate Course in Ophthalmology	Ohio State University College of Medicine 11th and Neil Aves., Columbus 10, Ohio	S	IO	Lec, AV	16	3/ 2/59	3/ 3/59	C; 2 days	20
Postgraduate Convention-Ophthalmology	Secretary-Treasurer, Oregon Academy of Ophthalmology and Otolaryngology 1216 S. W. Yamhill St., Portland 5, Ore.; course at University of Oregon School of Medicine, Portland, Ore.	S	IC	Lec, Pan, O, AV	16	6/29/59	6/30/59	C; 2 days	60, or 90 if combined with otol. course
Slit-Lamp Microscopy, Gonioscopy, Eye Surgery	Dr. H. E. Thorpe Committee on Ophthalmic Postgraduate Education, Montefiore Hospital, 3459 5th Ave., Pittsburgh 13;	S Lim 35	IO	Lab, PD, Sem, Lec, AV, EPP	28	5/ 4/59	5/ 7/59	C; 4 days	85
Biomicroscopy of the Posterior Vitreous and Fundus	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at The University of Texas M. D. Anderson Hospital Houston, Tex.	S and residents Lim 8	II	Lab, PD, Lec, AV	8	12/ 4/58	12/18/58	I; 3 sessions 1 hr. weekly, Thursdays	Nil

OPHTHALMOLOGY AND OTOLARYNGOLOGY

Otolaryngology and Ophthalmology Including Refraction and EENT (Cadaver)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 10	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	480	10/ 1/58 4/ 1/59	12/31/58	C; 72 days	600
Ophthalmology-Otolaryngology	University of Oklahoma Medical Center 801 N. E. 13th St., Oklahoma City	S	IC	PD, Sem, Lec, Pan, O, AV	8	3/12/59	3/13/59	C; 2 days	10
Postgraduate Convention-Ophthalmology and Otolaryngology	Secretary-Treasurer, Oregon Academy of Ophthalmology and Otolaryngology 1216 S. W. Yamhill St., Portland 5, Ore.; course at University of Oregon School of Medicine, Portland, Ore.	S	IC	Lec, Pan, O, AV	16	6/26/59	6/30/59	C; 4 days	90
Thirty-Second Annual Spring Congress in Ophthalmology and Otolaryngology	Gill Memorial Eye, Ear and Throat Hospital 711 S. Jefferson St., Roanoke, Va.	S Lim 200	IC	Lab, PD, LC, Clin C, Sem, Surg, Lec, O, AV, TV	40	4/ 6/59	4/11/59	C; 5½ days	80

ORTHOPEDIC SURGERY

(See also Anatomy, Fractures, General Practice, Surgery)

872 Orthopedics in General Practice	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Hotel Statler, Los Angeles	G	IO	PD, LC, Lec, Pan, O	24	Spring/59		C; 3 days	75
Orthopedic Basic Science	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 16	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	750	7/ 1/59	12/31/59	C; 120 days	600
[illegible]dics	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	Unknown	IC	PD, Lec, O, AV	7	2/25/59	2/25/59	C; 1 day	10
Orthopedic Surgery 1	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Children's Hospital, Boston	S Lim 2	IO	Lab, PD, LC, BR, Sem, Surg, Lec	Variable	Arranged		Arranged	800 for 12 mo.
Orthopedic Surgery 2	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	S Lim 2	IO	Lab, PD, LC, BR, Sem, Surg, Lec	Variable	Arranged		Arranged	800 for 12 mo.
Orthopedic Surgery-Herniated Disk, Skeletal Tuberculosis, Fractures of Spine	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N.J.; course at Hospital for Crippled Children, Newark, N.J. New Jersey Orthopaedic Hospital, Orange, N.J.	S Lim 35	II	PD, Lec, O, AV	15	10/11/58	12/10/58	I; 10 sessions 1½ hr. weekly Tuesdays	100

Key will be found on page 1954.

ORTHOPEDIC SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Orthopedic Surgery PM 81—Foot Disability	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Hospital for Joint Diseases, New York 35	G	II	PD, Lec, O, AV	21	10/ 2/58	10/ 4/58	I; 3 sessions 7 hr. thrice weekly Thursday, Friday, Saturday	100
Orthopedic Surgery PM 80	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Hospital for Joint Diseases, New York 35	G	IC	PD, Lec, O, AV	36	10/20/58	10/25/58	C; 6 days	100
Orthopedic Surgery PM 1—Musculo Skeletal Disease and Injury	Columbia University College of Physicians and Surgeons 630 W 168th St, New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	IC	Lec, O	35	1/ 5/59	1/ 9/59	C; 5 days	100
584-A Orthopedics for the General Practitioner	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 20	II	PD, BR, O, AV, EPP	16	10/ 7/58	12/ 2/58	I; 8 sessions 2 hr weekly, Tuesdays	45
586-A Orthopedic Aspects of the Treatment of Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave, New York 16	G Lim 20	II	PD, LC, BR, Clin C, Lec, O, AV	20	10/ 8/58	12/10/58	I; 10 sessions 2 hr. weekly, Wednesdays	50
582-A Orthopedics in General Practice	New York University Post Graduate Medical School 550 First Ave, New York 16	G Lim 20	IC	PD, BR, O, AV, EPP	21	2/18/59	2/20/59	C; 3 days	55
585-A Orthopedic Aspects of the Treatment of Rheumatic Disorders	New York University Post-Graduate Medical School 550 First Ave, New York 16	G Lim 20	II	PD, LC, BR, Clin C, Lec, O, AV	21	3/17/59	3/31/59	I; 3 sessions 7 hr. weekly, Tuesdays	50
Pathology and Roentgenology of the Skeletal System	Assistant to the Dean University of Wisconsin Medical School 418 N Randall Ave, Madison 6, Wis	S Lim 100	IC	PD, Lec, Pan, O, AV	21	5/21/59	5/23/59	C; 3 days	35

OTOLARYNGOLOGY

(See also Anatomy, Endoscopy, Pathology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Ear, Nose and Throat	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	PD, Sem, Lec, Pan, O, AV	12	3/ 7/59	3/ 8/59	C; 1½ days	50
Clinical Otolaryngology	Cook County Graduate School of Medicine 707 S Wood St, Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Surg, O	50	Arranged by appointment	2 wk later	10 days	50
Fellowship Fenestration Surgery	Northwestern University Medical School 303 E Chicago Ave, Chicago 11	S Lim 2	IC	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec	960	Arranged		C; 80 days	500
Endaural Otologic Surgery and Audiology	Northwestern University Medical School 303 E Chicago Ave, Chicago 11	S Lim 10	IC	Lab, PD, LC, BR, Clin C, Sem, Lec	200	3/59		C; 5 wk.	800
Annual Otolaryngologic Assembly—Current trends in Otolaryngology	University of Illinois College of Medicine 1853 W Polk St, Chicago 12	S Lim 40	IC	Lab, PD, Clin C, Sem, Lec, Pan, O, AV	61	9/29/58	10/ 5/58	C; 7 days	125
Basic Science of Otolaryngology	University of Illinois College of Medicine 1853 W Polk St, Chicago 12	Unknown Lim 20	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV	1584	10/ 1/58	6/30/59	190 days	750
Fundamentals of Otolaryngology for Otolaryngologists	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S	II	PD, LC, Clin C, Lec, O, AV	70	10/22/58	6/24/59	I; 35 sessions 2 hr weekly, Wednesdays	Nil
Anatomical and Clinical Aspects of Otolaryngology	Indiana University School of Medicine 1100 W Michigan St, Indianapolis 7	S Lim 20	IC	Lab, PD, LC, Lec, Pan, O, AV	100	4/ 6/59	4/18/59	C; 13 days	250
Clinical Traineeship in Otorhinolaryngology	University of Kansas Medical Center 39th and Rainbow Blvd, Kansas City, Ks	G Lim 1	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP		Arranged	1 mo later	30 days	50 in state; 100 out of state
Otolaryngology	University of Kansas Medical Center 39th and Rainbow Blvd, Kansas City, Ks	S	IC	PD, Clin C, Lec, Pan, O, AV	17	4/ 6/59	4/ 8/59	C; 3 days	40
Otolaryngology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich	S Lim 60	IC	PD, Lec, O, AV	18	4/16/59	4/18/59	C, 3 days	50
Otolaryngology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	15	1/ 5/59	1/ 7/59	C; 3 days	40
Otolaryngology for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota	S	IC	Lec, O, AV	15	5/27/59	5/29/59	C, 3 days	40

Home Study Course in Otolaryngology	American Academy of Ophthalmology and Otolaryngology 15 Second St., S. W., Rochester, Minn.	S	HS (R)	Assigned reading		9/ 1/58	6/30/59	9 mo	25
Medical Otolaryngology and Related Allergy and Immunology	Hansel Foundation 631 N. Grand Ave., St. Louis	S Lim 60	IC	Lab, Lec, Pan, O, AV, EPP	40	5/25/59	5/29/59	C; 5 days	150
Otorhinolaryngology PM 30—Transmeatal (endaural) Surgery	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S Lim 8	IC	Lab, Surg, Lec, O, AV, EPP	50	9/ 8/58 1/ 6/59	9/19/58	C; 10 days	300
Otorhinolaryngology PM 31—Mobilization of Stapes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 4	IC	Lab, PD, Surg	120	11/ 3/58 1/ 6/59	11/21/58	C; 15 days	500
Otorhinolaryngology PM 32—Voice Rehabilitation and Audiology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	IC	PD, LC, Sem	12	2/ 9/59 2/12/59	2/11/59	C; 3 days	75
Otolaryngology PM 2—Histopathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lab	32	4/ 7/59	5/28/59	I; 16 sessions 2 hr. twice weekly, Tuesdays, Thursdays	100
591-A. Endaural Surgery	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 8	IC	Lab, PD, Sem, Lec, Pan, O, AV, EPP	70	11/ 3/58 1/26/59	11/14/58	C; 10 days	250
5910 A. Laryngology and Surgery of the Larnyx and Neck	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 10	IC	Lab, PD, LC, Sem, Surg, Lec, Pan, O, AV, EPP	70	1/ 5/59	1/16/59	C; 10 days	250
5912-A. Seminar in Recent Advances in Otolaryngology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 15	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	35	2/16/59	2/20/59	C; 5 days	75
597-A Audiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 15	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV, EPP	35	3/ 2/59	3/ 6/59	C; 5 days	100
598-A. Neuro-Otology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 10	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	21	3/ 9/59	3/11/59	C; 3 days	50
Ninth Annual Teaching Day in Otolaryngology	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	S	IC	Sem, Lec, Pan, AV	8	Spring/59		C; 1 day	Unknown
Postgraduate Convention-Otolaryngology	Secretary-Treasurer, Oregon Academy of Ophthalmology and Otolaryngology 1216 S.W. Yamhill St., Portland 5, Ore.; course at University of Oregon School of Medicine, Portland, Ore	S	IC	Lec, Pan, O, AV	16	6/26/59	6/27/59	C; 2 days	60 or 90 if combined with Oph. course
Anatomy, Diagnosis and Treatment of Laryngeal Disease and Laryngeal Surgery	Chevalier Jackson Clinic, Temple University Medical Center 3401 N. Broad St., Philadelphia 40	B Lim 6	IC	Lab, PD, LC, Clin C, Sem, Surg, Pan, O, AV, EPP	80	12/ 1/58	12/12/58	C; 11 days	250
Myringoplasty	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.	S Lim 12	IC	PD, BR, Surg, Lec, AV	21	3/26/59	3/28/59	C; 3 days	50
Rehabilitation of the Laryngectomee	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	G also non-physicians Lim 30	IC	PD, Lec, O, EPP	50	6/59		C; 10 days	Nil

PATHOLOGY

(See also Clinical Pathology, Malignant Disease)

Surgical Pathology	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G Lim 15	II	Lec	178	9/ 9/58	6/ 4/59	I; 71 sessions 2½ hr. twice weekly, Tuesdays, Thursdays	175
Neuropathology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S Lim 40	II	Lec, O	16	9/24/58	11/12/58	I; 16 sessions 1 hr. weekly, Wednesdays	Nil

Key will be found on page 1934.

PATHOLOGY - Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pathology 200—Brain Tumor Registry	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S Neurosurgery, Neurology and Neuropathology Lim	IC	Sem, O, AV	Arranged	Arranged		Arranged	Arranged
Application of Histochemistry to Pathology	Armed Forces Institute of Pathology 6825 - 16th St., N.W., Washington 12, D. C.	S Lim 30	IC	Lab, Sem, Lec		10/27/58	10/31/58	C; 5 days	Nil
Ophthalmic Pathology	Armed Forces Institute of Pathology 6825 - 16th St., N.W., Washington 12, D. C.	S Lim 50	IC	Lab, Sem, Lec, AV	45	3/ 9/59	3/13/59	C; 5 days	Nil
Pathology of the Oral Regions	Armed Forces Institute of Pathology 6825 - 16th St., N.W., Washington 12, D. C.	B and dentists Lim 100	IC	Sem, Lec, Pan	36	3/23/59	3/27/59	C; 5 days	Nil
Cardiovascular Pathology Seminar	Armed Forces Institute of Pathology 6825 - 16th St., N.W., Washington 12, D. C.	B Lim 125	IC	Sem	32	4/ 6/59	4/10/59	C; 5 days	Nil
Gynecological Pathology Review	Baptist Memorial Hospital 800 Miami Road, Jacksonville, Fla.	S Lim 20	II	Sem, Lec, O, AV	9	2/ 5/59	3/26/59	I; 6 sessions 1½ hr. weekly, Wednesdays	Nil
Surgical Pathology Review	Baptist Memorial Hospital 800 Miami Road, Jacksonville, Fla.	S Lim 20	II	Sem, Lec, O, AV	9	4/ 2/59	5/ 7/59	I; 6 sessions 1½ hr. weekly, Wednesdays	Nil
Surgical Pathology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 9	IC	Lab, Clin C, Sem, Lec, O, EPP	48	Arranged By appointment	2 wk. later	C; 12 days	150
Surgical Pathology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 9	IC	Lab, Clin C, Sem, Lec, O, EPP	96	Arranged appointment	4 wk. later	C; 24 days	250
Orthopedic Pathology—Bone Disease	Indiana University School of Medicine 1100 W Michigan St., Indianapolis 7	G	II	Lab, Lec, O, AV, EPP	22	10/ 6/58	12/15/58	I; 11 sessions 2 hrs. weekly, Mondays	50
Clinical Traineeship in Pathology	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	Lab, PD, Clin C, Sem, Lec, O, AV EPP	Varies	Arranged	at least 1 mo. later	Arranged	50 per mo. in state; 100 per mo. out of state
Neuropathology	University of Maryland School of Medicine Lombard and Greene Sts., Baltimore	S Lim 3	IC	Lab, Sem		Arranged	six mo. later	C; six mo. full time	210
Pathology of Tuberculosis	Wayne State University College of Medicine 1402 Rivard St., Detroit; course at Herman Kiefer Hospital, Detroit	S Lim 15	II	Lab, PD, Sem, Lec, AV, EPP	36	12/10/58	3/11/59	I; 12 sessions 3 hr. weekly, Wednesdays	50
Gynecological and Obstetrical Pathology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Kings County Hospital, Brooklyn, N. Y.	S Lim 10	II	Lec, AV	30	3/59	5/59	I; 10 sessions 3 hr. weekly, Fridays	100
Pathology GM 1-Surgical Pathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G	PT	Lab, PD, Clin C, EPP		1st day ea. mo.		6 or 12 mo.	300 for 6 mo. 600 for 12 mo.
Pathology PM 30-General and Special Pathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	II	Lab	30	9/20/58	1/10/59	I; 15 sessions 2 hr. weekly, Saturdays	100
Pathology PM 31-Surgical Pathology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lab	30	1/10/59	4/18/59	I; 15 sessions 2 hr. weekly, Saturdays	100
Exfoliative Cytology	Cornell University Medical College 1300 York Ave., New York 21	S also Pathology technologists Lim 32	IC	Lab, Lec, O, AV, EPP	396	3/ 9/59	5/29/59	C; 66 days, shorter by arrangement	360
Surgical Pathology	New York Polyclinic Hospital	G	IC	Lab, PD, I C, Clin C, Lec	360	10/ 1/58	12/31/58	C; 72 days	300

PEDIATRICS

(See also Dermatology, Cardiovascular Disease, Endocrinology, Lphebology, Neurology, Occupational Medicine Psychiatry)

agnosis	Department of Continuing Education in Medicine and Health Sciences University of California at Los Angeles Medical Center, Los Angeles 24	G	IO	PD, Sem, Lec, Pan, O, AV	12	12/58		C; 2 days	Unknown
Short Term Clinical Course in Pediatrics	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Children's Hospital, Los Angeles	G	PT	PD, LC, BR, Sem, Lec, LPP		Arranged	Arranged	Arranged	150 for 2 wk.; 200 for 4 wk.; 250 for 6 wk.;
Speech Problems	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Children's Hospital, San Francisco	G Lim 75	IO	PD, Lec, Pan, O, AV	7	11/15/58	11/15/58	C; 1 day	12 50
Clinical and Research Advances in Child Guidance Problems	University of Colorado School of Medicine 4200 E. Ninth Ave. Denver 20, course at Stanley Hotel, Estes Park, Colo	S Lim 350	IO	Sem, Lec, Pan, O, AV	36	9/ 4/58	9/ 9/58	C; 1½ days	55 or 35 for each part
Pediatric Postgraduate Day	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B Lim 100	II	PD, LC, Sem, Lec, Pan, O, AV	36	10/ 3/58	6/ 5/59	I; 9 sessions 4 hr monthly, 1st Friday each mo	Nil
Clinical Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St. Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Sem, O, EPP	60	Arranged by appointment	2 wk later	12 days	60
Clinical Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 4	PT	Lab, PD, LC, BR, Clin C, Sem, O, EPP	120	Arranged by appointment	4 wk later	21 days	100
Course V—Pediatrics	Cook County Graduate School of Medicine 707 S. Wood St. Chicago 12	G Lim 25	IO	Lab, PD, LC, BR, Clin C, Sem, Lec, O	70	4/20/59	5/ 1/59	C, 11 days	150
Pediatrics for General Physicians	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IO	Lec, Pan, O, AV	7	12/17/58	12/17/58	C, 1 day	10
Pediatric Course	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IO	PD, BR, Lec, Pan, O, AV	12	9/17/58	9/18/58	C; 2 days	20
Clinical Traineeship in Pediatrics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G Lim 2	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, O, EPP	Varies	Arranged	1 mo later	Arranged	50 in state; 100 out of state
Pediatrics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IO	PD, Clin C, Lec, Pan, O, AV	21	3/ 9/59	3/11/59	C; 3 days	40
Annual Pediatric Postgraduate Course	Department of Pediatrics, Univ. of Louisville Medical School 323 E. Chestnut St., Louisville 2; course at The Children's Hospital, Louisville 2	G Lim 50	II	PD, Clin C, Sem, Lec, Pan, O, AV	22	4/14/59	6/ 2/59	I; 8 sessions 3 hr weekly, Tuesdays	30
Pediatric Dermatology	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	S Lim 10	IO	PD, Sem, Lec, Pan, O	44	2/16/59	2/21/59	C; 5½ days	50
Pediatric Metabolism and Endocrinology	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston 14	G	IO	PD, Lec	28	Probably autumn 1958		C; 4 days	70
Pediatrics 2	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Children's Hospital, Boston 15	G Lim 8	IO	Lab, PD, LC, BR, Clin C, Lec, Pan, O	420	10/ 1/58 2/ 3/59	1/23/59	C; 14 wk	500
Pediatrics 3	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	G Lim 50	IO	PD, Clin C, Lec	70	Probably 6/59		C; 11 days	150
Pediatrics	New England Medical Center 171 Harrison Ave., Boston	G Lim 50	IO	PD, LC, Clin C, Sem, Pan, O	16	3/19/59	3/21/59	C; 3 days	20

Key will be found on page 1954.

PEDIATRICS—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pediatrics	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	18	1/26/59	1/28/59	C; 3 days	30
Institute on Maternal and Child Health and Crippled Children	University of Minnesota School of Public Health and University of Michigan School of Public Health; course at Minneapolis	Child Health M.D.'s, Nurses, Social Workers Lim 72	IC	Sem, Lec, Pan, O	40	12/ 1/58	12/ 5/58	C; 5 days	Nil
Pediatrics for Pediatricians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Lec, Pan, O, AV	15	9/23/58	9/25/58	C; 3 days	40
Pediatrics for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	15	3/ 2/59	3/ 4/59	C; 3 days	40
In Hospital Review In Pediatrics	University of Nebraska College of Medicine 42nd and Dewey, Omaha 5	G Lim 5	PT	PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	40	Unknown		5½ days	50
Pediatrics	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	PD, BR, Clin C, Sem, Lec, Pan, O, AV	12	4/13/59	4/14/59	C; 2 days	20
Emotional and Psychiatric Aspects of Pediatrics	Seton Hall College of Medicine and Dentistry, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at St. Michael's Hospital Newark, N. J.	B Lim 45	II	Lec, O, AV	15	1/14/59	3/18/59	I; 10 sessions 1½ hr. weekly, Wednesdays	25
Pediatric Teaching Day	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	12/11/58	12/11/58	C; 1 day	10
Pediatric Refresher Course	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G Lim 25	II	PD, LC, BR, Clin C, Sem, O	24	3/26/59	4/30/59	I; 6 sessions 4 hr. weekly, Thursdays	30
Management of Infectious Diseases in Children	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 12	II	BR, Lec	24	10/15/58	12/31/58	I; 12 sessions 2 hrs. weekly, Wednesdays	25
Lecture Course on the Common Problems in Office Pediatrics	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at South Nassau Communities Hospital, Oceanside, N. Y.	G	II	Lec	8	12/ 3/58	1/15/59	I; 8 sessions 1 hr. weekly, Wednesdays	15
Tumors of Childhood	Memorial Center for Cancer and Allied Diseases 444 E. 68th St., New York	B	II	PD, BR, Sem, Lec, AV	16	9/58 11/58 1/59 4/59	11/58	I; 2 hr. weekly, Fridays	Nil
Pediatric Oncology—Tumors, Leukemia, Related Pediatric Diseases	Memorial Center for Cancer and Allied Diseases 444 E. 68th St., New York	B Lim 15	IC	Lab, PD, BR, Sem, AV	24	4/27/59	4/30/59	C; 3 days	35
Pediatrics	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 8	IC	Lab, PD, LC, BR, Clin C, Lec, O	144	10/ 1/58 4/59	10/31/58	C; 24 days	100
616-A. Seminar on General Pediatrics	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	II	LC, Clin C, Sem, Lec, Pan, AV	36	10/ 1/58	5/27/59	I; 18 sessions 2 hr. weekly, Wednesdays	Unknown
612-A. Pediatric Endocrinology and Related Metabolism	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	Lab, PD, Clin C, Lec, AV	24	11/10/58	11/13/58	C; 4 days	85
613-A. Pediatric Cardiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	IC	PD, LC, BR, Clin C, Lec, O, AV	35	12/ 1/58	12/ 5/58	C; 5 days	55
614-A. Symposium on Tuberculosis and Other Pulmonary Diseases in Childhood	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, Clin C, Sem, Lec, Pan, O, AV	35	4/13/59	4/17/59	C; 5 days	65
Pediatrics for the Family Physician	Rochester General Hospital 501 W. Main St., Rochester, N. Y.	G	II	PD, LC, Clin C, Sem, Lec, Pan, AV	8	1/22/59	1/29/59	I; 2 sessions 4 hr. weekly, Thursdays	10
Problems In Pediatric Practice	State University of New York Upstate Medical Center 766 Irving Ave., Syracuse, N. Y.	B Lim 20	IC	PD, Sem, O, AV	14	4/ 9/59	4/10/59	O; 2 days	10
The Letchworth Graduate Course in Mental Retardation	Program Director, Research Foundation for Mental Hygiene, Inc. Letchworth Village, Thiells, N. Y.	B Lim 10	IC	Lab, PD, LC, Clin C, Sem, Lec, O, AV	114	11/ 3/58 12/ 1/58 3/ 9/59 4/ 6/59	11/22/58	C; 16½ days	Nil

Home and Office Pediatrics	Dr. Gaston B. Hannah Southwestern Ohio Society of General Physicians Sharon and Willow Aves., Glendale, O.; course at University of Cincinnati College of Medicine, Cincinnati 29	G	IO	Sem, Pan	•	11/10/58	11/10/58	C; 1 day	10
Refresher Course for General Practitioners	The Children's Hospital of Philadelphia 1740 Bainbridge St., Philadelphia 46	G Lim 50	II	PD, LC, BR, Clin C, Sem, Lec, Pan, O	48	3/18/59	6/ 3/59	I; 12 sessions 1 hr. weekly, Wednesdays	120
Pediatric Advances	The Children's Hospital of Philadelphia 1740 Bainbridge St., Philadelphia 46	G Lim 100	IO	PD, LC, Clin C, Lec, Pan, O	35	5/25/59	5/29/59	C; 5 days	115
Recent Advances in Pediatrics for the General Practitioner	Hahnemann Medical College and Hospital 230 N. Broad St., Philadelphia	G Lim 25	II	PD, LC, BR, O, AV	24	9/58	Unknown	I; 12 sessions 2 hr. weekly, Wednesdays	50
Practical Pediatric Hematology	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 50	IO	PD, Clin C, Lec, Pan, O, AV	7	6/ 3/59	6 / 5/59	C; 3 days	75
Hemolytic Diseases of the Newborn	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 50	IO	PD, Clin C, Lec, Pan, AV	15	6/ 5/59	6/ 6/59	C; 2 days	50
A Postgraduate Review in Pediatrics	Vanderbilt University School of Medicine 21st Ave. South, Nashville, Tenn.	G	IO	PD, LC, Clin C, Lec, Pan, O	6	Fall/58	Fall/58	C; 1 day	15
Postgraduate Refresher Course in Pediatrics	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at Scott and White Memorial Hospitals Scott, Sherwood and Brindley Foundation, Temple, Tex.	G Lim 1	IO	PD, LC, BR, O, EPP	176	1st. Monday of each mo. January through December	Last Saturday of mo.	C; 24 days	25
The Brain Damaged Child	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B Lim 270	IO	Lec, Pan, O, AV, TV	20	1/ 8/59	1/10/59	C; 3 days	5
Problems of the Newborn Period	Assistant to the Dean University of Wisconsin Medical School 418 N. Randall Ave., Madison 6, Wis.	G Lim 100	IO	PD, Lec, Pan, O, AV	18	2/19/59	2/21/59	C; 2½ days	30

PERIPHERAL VASCULAR DISEASE

(See also Surgery)

Peripheral Vascular Disease	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IO	PD, Sem, Lec, Pan, O, AV		Spring/59		Unknown	Unknown
Peripheral Vascular Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IO	PD, BR, Sem, Lec, Pan, O, AV	11	2/18/59	2/19/59	C; 2 days	30
Peripheral Vascular Diseases	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 20	II	Lec, AV	10	10/58	12/58	I; 10 sessions 1 hr. weekly, Mondays	20
Peripheral Vascular Diseases	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Hospital of Brooklyn, Brooklyn, N. Y.	G Lim 20	II	PD, Lec.	10	4/59	5/59	I; 10 sessions 1 hr. twice weekly, Mondays, Fridays	20
Medicine PM 65-Peripheral Vascular Diseases	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 15	II	PD, BR, Sem, Lec, O, AV, EPP	75	10/ 2/58	4/ 9/59	I; 25 sessions 3 hr. weekly, Thursdays	125
5415-A. Peripheral Vascular Diseases	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IO	PD, Lec	35	11/17/58	11/21/58	C; 5 days	60
5425-A. Peripheral Vascular Diseases	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	PD, Lec	18	1/ 7/59	5/26/59	I; 8 sessions 2 hr. weekly, Tuesdays	50
Peripheral Vascular Disease	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 5	II	Lec, AV	10	9/58	12/58	I; Unknown	25
Peripheral Vascular Diseases	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	G Lim 80	IO	Clin, C, Lec, Pan, O, AV	20	6/25/59	6/27/59	C; 3 days	75

Key will be found on page 1954.

PHYSICAL MEDICINE AND REHABILITATION

(See also Occupational Medicine, Otolaryngology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Physical Medicine and Rehabilitation	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	PD, Lec, Pan, O, AV	14	Spring/58		C; 2 days	40
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	B Lim 35	IC	PD, LC, Lec, Pan, O	36	9/29/58 1/ 5/59 4/ 6/59	10/ 3/58	C; 5 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	G Lim 18	IC	PD, LC, Lec, Pan, O, AV, EPP	480	9/29/58 1/ 5/59 4/ 6/59	12/19/58	C; 90 days	Nil
Physical Therapy and Occupational Therapy in the Care of Neuro-Muscular Disease	Georgia Warm Springs Foundation Warm Springs, Ga.	G Lim 18	IC	PD, LC, Lec, Pan, O, AV, EPP	960	9/29/58 1/ 5/59 4/ 6/59	3/27/59	C; 180 days	Nil
Clinical Traineeship in Physical Medicine	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 1	PT	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	Varies	Arranged	at least 1 mo. later	Arranged	50 per mo. in state; 100 per mo. out of state
Physical Medicine for Specialists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	PD, Lec, O, AV	15	11/20/58	11/22/58	C; 3 days	40
Physical Medicine and Rehabilitation	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey, Omaha	G	IC	PD, BR, Clin C, Sem, Lec, Pan, O, AV	6	2/26/59	2/26/59	C; 1 day	10
Physical Medicine and Rehabilitation	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Coney Island Hospital, Brooklyn, N. Y.	G Lim 20	II	Lec, AV	10	10/58 4/59	12/58	I; 10 sessions 1 hr. weekly, Thursdays	20
Physical Medicine and Rehabilitation GM 1	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	G	IC	PD, Clin C, AV		1st. day ea. mo.	6 or 12 mo. later		300 for 6 mo.; 600 for 12 mo.
Physical Medicine and Rehabilitation	New York Polyclinic Hospital 345 W. 50th St., New York 19	G	IC	PD, LC, BR, Lec, O	144	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	100
621-A. Physical Medicine and Rehabilitation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 30	IC	PD, Lec	70	1/ 5/59 5/ 4/59	1/16/59	C; 10 days	100
Physical Medicine and Rehabilitation Postgraduate Courses	Highland View Cuyahoga County Hospital 3901 Ireland Drive, Cleveland 22	S	PT	PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O		1/ 5/59 7/59	6/59	130 class days 6 mo.	Nil
PROCTOLOGY									
Proctology	Department of Continuing Education in Medicine and Health Sciences, University of California Medical Center Los Angeles 24	G	IC	Lab, PD, Sem, Surg, Lec, Pan, O, AV	6	11/58	Same day	C; 1 day	40 entire day; 10 lecture session only
Proctology	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	Lec, Pan, AV	7	11/ 8/58	11/ 8/58	C; 1 day	20
Proctology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G Lim 20	IC	Lec, O, AV	30	5/18/59	5/22/59	C; 5 days	65
Proctology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Jewish Hospital of Brooklyn, Brooklyn, N. Y.	G Lim 20	II	PD, LC, Lec	18	10/58	12/58	I; 12 sessions 1½ hr. twice weekly, Mondays, Fridays	30
Surgery PM 30—Office Proctology	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital New York 29	S	IC	Lec, O, AV	10	11/ 6/58 4/16/59	11/ 7/58	C; 2 days	25
Proctology (Clinical and Cadaver)	New York Polyclinic Hospital 345 W. 50th St., New York 19	G	IC	Lab, PD, LC, BR, Lec, O	60	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	175
Postgraduate Refresher Course in Proctology	University of Texas Postgraduate School of Medicine 1100 Outer Belt Drive Houston 25, Tex.	G Lim 2	IC	PD, LC, BR, Sem, Surg, O	88	Arranged		C; 12 days	25

Practice	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	G Lim 75-100	II	PD, Lec	20	Unknown		I; 10 sessions 2 hr. weekly, Wednesdays	50
Therapeutic Interviewing of Patients with Emotional Problems	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33; course at Los Angeles County Hospital, Los Angeles 33	B Lim 10	II	PD, LC, EPP	24	10/15/58	1/14/59	I; 12 sessions 2 hr. weekly, Wednesdays	100
Practical Psychiatry in General Hospitals	University of California Medical Center Second and Parnassus Ave., San Francisco; course at Herrick Memorial Hospital, Berkeley, Calif.	G Lim 50	IC	PD, Sem, Lec, Pan, O	14	Fall/58		C; 2 days	40
Psychopharmacology	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	Lec, Pan, O, AV	14	Winter/ 1958-59		C; 2 days	40
Basic Psychiatry and Psychology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Connecticut State Hospital, Middletown, Conn.	S Lim 50 to 70	II	Lec, O	66½	9/18/58	4/15/59	I; 30 sessions 2 hr. weekly, Wednesdays	Nil
Child Psychiatry	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S Lim 40	II	Lec, O	18	2/11/59	3/18/59	I; 12 sessions 1½ hr. weekly, Wednesdays	Nil
Experimental Basis of Psychiatric Theory	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	S Restricted to military personnel Lim 15	IC	Lab, BR, Sem, Lec, O	160	2/ 9/59	3/ 6/59	C; 20 days	Nil
Forces in the Family; Emotional Interrelationships between Family Members	North Shore Hospital 225 Sheridan Road, Winnetka, Ill.	G	II	Lec, O, AV	18	10/ 1/58	6/ 3/59	I; 9 sessions 2 hr. mo. First Wednesday	Nil
Psychiatry for General Physicians	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G	IC	PD, Lec, Pan, O, AV	11	11/19/58	11/20/58	C; 2 days	15
Clinical Traineeship in Psychiatry	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	PD, LC, BR, Clin C, Sem, Lec, O, AV, EPP	Varies	Arranged	at least 3 mo. later	Arranged	50 per mo. in state; 100 per mo. out of state
Pharmacology & Psychiatry Drugs Affecting Emotions	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IC	Sem, Lec, Pan, O	20	11/20/58	11/22/58	C; 2½ days	25
Basic Literature in Psychiatry, Chiefly psychoanalytic	Spring Grove State Hospital Wade Ave., Catonsville 28, Md.	S Lim 35	II	Sem, Lec, O	20	Unknown		I; 10 sessions 2 hr. weekly	35
Personality Development	Spring Grove State Hospital Wade Ave., Catonsville 28, Md.	S Lim 35	II	Sem, Lec, O	20	9/ 2/58	1/20/59	I; 10 sessions 2 hr. biweekly, Tuesdays	35
Psychiatry in General Practice	Office of Postgraduate Affairs University of Nebraska College of Medicine, 42nd and Dewey, Omaha	G	IC	Sem, Lec, Pan, O, AV TV, R	6	12/ 4/58	12/ 4/58	C; 1 day	Unknown
The Physician's Role in Mental Health	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 30	II	Lec, Pan, O	15	Unknown		I; 10 sessions 1½ hr. each	Unknown
Management of Psychiatric Problems in General Practice	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IC	PD, Sem, Lec, Pan, O, AV	14	10/29/58	10/30/58	C; 2 days	30
Psychotherapy in Everyday Practice	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 15	II	Lec	15	10/ 1/58	12/ 3/58	I; 10 sessions 1½ hrs. weekly, Wednesdays	35
Intensive Psychotherapeutic Medicine	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 10	II	Sem	30	1/ 7/59	5/20/59	I; 20 sessions 1½ hr. weekly, Wednesdays	50

Key will be found on page 1954.

HIATRY—Continued

of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Title Contributions to	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	22	9/ 8/58	12/15/58	I; 15 sessions 1½ hr. weekly, Mondays	60
Physical Medicir ychoanalysis. The Physical Therapyd	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	30	9/ 9/58	1/27/59	I; 20 sessions 1½ hr. weekly, Tuesdays	80
Therapy in the Neuro-Muscu nferences on Case Physical ories I	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Sem	15	9/12/58	11/14/58	I; 10 sessions 1½ hr. weekly, Fridays	40
Problems in Therapy	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 15	II	Sem	15	9/12/58	11/14/58	I; 10 sessions 1½ hr. weekly, Fridays	50
Continuous Case Seminar— Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem	18	9/ 9/58	11/25/58	I; 12 sessions 1½ hr. weekly, Tuesdays	60
Fundamentals of Psychoanalytic Technique	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	30	9/ 8/58	1/26/59	I; 20 sessions 1½ hr. weekly, Mondays	80
Neuroses and Psychoses	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Lec	22	9/29/58	1/12/59	I; 15 sessions 1½ hr. weekly, Mondays	27
Psychoanalytic Workshop on Human Behavior	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Sem	22½	9/30/58	1/13/59	I; 15 sessions 1½ hr. weekly, Tuesdays	27
Seminar on Child Therapy, Psychoanalytic	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem, Lec	10½	11/21/58	1/16/59	I; 7 sessions 1½ hr. weekly, Fridays	28
Readings in Psychoanalytic Pioneers	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	22½	2/ 2/59	5/18/59	I; 15 sessions 1½ hr. weekly, Mondays	60
The Psychoanalytic Process	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem, Lec	22½	2/ 2/59	5/18/59	I; 15 sessions 1½ hr. weekly, Mondays	75
Clinical Conferences—Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 10	II	Sem	15	2/ 3/59	4/ 6/59	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Theory of Neurosis	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Lec	22	2/ 3/59	5/18/59	I; 15 sessions 1½ hr. weekly, Tuesdays	60
Body Involvement in Emotional Conflict	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Lec	22½	2/ 5/59	5/18/59	I; 15 sessions 1½ hr. weekly, Mondays	27
Body Involvement in Emotional Conflict	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Lec	22½	2/ 5/59	5/18/59	I; 15 sessions 1½ hr. weekly, Mondays	27
Clinical Conferences on Case Histories II	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 20	II	Sem	15	2/ 6/59	4/10/59	I; 10 sessions 1½ hr. weekly, Fridays	40
Workshop on Dreams	American Institute for Psychoanalysis 220 W. 98th St., New York	S Lim 30	II	Sem	15	2/ 6/59	4/10/59	I; 10 sessions 1½ hr. weekly, Fridays	50
Group Psychodynamics and Group Psychoanalysis	American Institute for Psychoanalysis 220 W. 98th St., New York; course at New School for Social Research, New York	G Lim 50	II	Lec	22½	2/10/59	5/19/59	I; 15 sessions 1½ hr. weekly, Tuesdays	27
Growth and Development of Personality from Infancy Through Adolescence	Dr. Harold Jacobziner, Assistant Commissioner New York City Department of Health 125 Worth St., New York	G Lim 40	II	Lec	24	4/59	6/59	I; 8 sessions 3 hr. weekly, Mondays	Nil
701 The Development of Psycho- analytic Thinking	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S also Ph.D Psychol., M.S. Social Workers	II	LC, Lec	24	9/29/58 2/ 9/59 (Part II)	1/19/59	I; 16 sessions 1½ hr. weekly, Mondays	60

								1½ hr. weekly, Tuesdays	
Comprehensive Curriculum in Group Psychotherapy	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S also Ph.D. Psychol., M.S. Social Workers Lim 15	II	LC, Sem	Fall 60 Spring 68	9/30/58 2/10/59	6/ 6/59	I; Weekly, Tuesdays	500 per yr.
731 Clinical Conferences	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	7½	10/ 1/58 3/11/59	10/29/58	I; 5 sessions 1½ hr. weekly, Wednesdays	20
715 Introduction to Psychotherapy and Psychotherapeutic Techniques	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Lec	18	10/ 1/58	12/17/58	I; 12 sessions 1½ hr. weekly, Wednesdays	60
717 Clinical Conferences	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	22½	10/ 1/58	12/ 3/58	I; 15 sessions 1½ hr. weekly, Wednesdays	40
710 Seminar: Psychosomatic Medicine	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	G also Ph.D. Psychol. Lim 25	II	LC, Lec	22½	10/ 2/58	1/29/59	I; 15 sessions 1½ hr. weekly, Thursdays	60
706 Techniques of Dream Interpretation	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	15	10/ 2/58	12/11/58	I; 10 sessions 1½ hr. weekly, Thursdays	40
733 Seminar: Psychosomatic Illness in Psychotherapeutic Practice	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	G Lim 25	II	LC, Lec	12	10/ 6/58 2/16/59	1/ 9/59	I; 8 sessions 1½ hr. weekly, Mondays	40
725 Audio Visual Techniques	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	Staff in Center but open to professional guests	II	LC, AV	12	11/24/58	1/19/59	I; 8 sessions 1½ hr. weekly, Mondays	Nil
724 Orientation into Projective Testing for Psychiatrists and Psychiatric Case-workers	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Lec	7½	12/10/58	1/14/59	I; 5 sessions 1½ hr. weekly, Wednesdays	20
727 Orientation into Social Casework for Psychiatrist and Psychologists	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S also Ph.D. Psychol., M.S. Social Workers Lim 25	II	LC, Lec	7½	12/18/58	1/29/59	I; 5 sessions 1½ hr. weekly, Thursdays	20
817 Clinical Conferences: Character Disorders	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	15	2/ 9/59	4/27/59	I; 10 sessions 1½ hr. weekly, Mondays	40
818 The Borderline Patient	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	22½	2/11/59	5/27/59	I; 15 sessions 1½ hr. weekly, Wednesdays	60
800 Continuous Case Seminar	Postgraduate Center for Psychotherapy 218 E. 70th St., New York	S Lim 25	II	LC, Sem	12	3/18/59	5/19/59	I; 8 sessions 1½ hr. weekly, Wednesdays	40
Postgraduate Medicine II—Psychoanalysis	Western Reserve University School of Medicine Hanna Pavilion, 2010 Abington Rd., Cleveland	S Lim 15	II	Sem	30	10/58	7/59	I; 20 sessions 1½ hr. every 2 wk., Tuesdays	Nil
Psychiatric Problems Handled by the General Practitioner	Dr. Gaston B. Hannah, Secretary Southwestern Ohio Society of General Physicians Sharon and Willow Aves., Glendale, O.; course at University of Cincinnati College of Medicine, Cincinnati 29	G	IC	Sem, Lec, Pan, O, AV	8	3/ 1/59	3/ 1/59	C; 1 day	10
Psychotherapy for Physicians	University of Pittsburgh School of Medicine Staunton Clinic—3601 Fifth Ave., Pittsburgh 13	G Lim 16	II	Sem, O, EPP	30	10/ 1/58 1/ 7/59 3/18/59	12/10/58	I; 10 sessions 2 hr. weekly, Wednesdays or Thursdays	40
Psychoanalytic Psychiatry	Vermont State Hospital Waterbury, Vt.	S	II	PD, Sem, Lec	8	9/58 11/58	4/59	I; 4 sessions 2 hr. weekly, Thursdays	Nil

PULMONARY DISEASE

(See also Internal Medicine, Radiology)

11th Annual Symposium on Pulmonary Diseases	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20; course at Fitzsimons Army Hospital, Denver, Colo.	B	IC	PD, Sem, Lec, Pan, O, AV	40	9/ 8/58	9/12/58	C; 5 days	[illegible]

Key will be found on page 1954.

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PULMONARY DISEASE—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Pulmonary Emphysema	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	G Lim 50	IC	Lec, Pan, O, AV	6	1/ 7/59	1/ 7/59	C; 1 day	10
Clinical Traineeship in Pulmonary Disease	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G Lim 2	PT	Lab, PD, LC, BR, Clin C, Sem, Lec, AV, EPP	160	11/ 3/58 1/ 2/59 4/ 1/59 5/ 1/59	11/29/58	30 days	50 per mo. in state; 100 per mo. out of state
Pulmonary Disease Clinic	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, BR, Lec, Pan, O, AV	14	1/19/59	1/20/59	C; 2 days	30
The Measurement of Pulmonary Function in Health and Disease	American Trudeau Society, Edward J. Welch, M.D., Chairman 1101 Beacon St., Brookline, Mass.; course at Boston City Hospital, Boston	S Lim 150	IC	PD, Clin C, Sem, Lec, Pan, O, AV	35	3/23/59	3/27/59	C; 5 days	75
Pulmonary Diseases	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 60	IC	PD, Clin C, Lec, Pan, O, AV	35	3/16/59	3/20/59	C; 5 days	50
Pulmonary Insufficiency	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, O, AV	6	11/20/58	11/20/58	C; 1 day	12
Eighth Annual Symposium for General Practitioners on Tuberculosis and Other Chronic Pulmonary Diseases	Trudeau Foundation 7 Church St., Saranac Lake, N. Y.; course also at Ray Brook State Tuberculosis Hospital, Ray Brook, N. Y.	G Lim 75	IC	PD, LC, BR, Lec, Pan, O	26	Summer/59		C; 5 days	50

RADIOISOTOPES

(See also Radiology)

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
882 b Practical Experience in the Laboratory Techniques Needed for Working with Radioactive Isotopes	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S Lim 2	PT	Lab		Arranged		Arranged	350
882 c Supervised Clinical Experience with Radioactive Isotopes	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S Lim 2	PT	PD, LC, BR	Unknown	Arranged		Arranged	165
882 a Lectures in the Physics and Clinical Application of Radioactive Isotopes	University of Southern California School of Medicine Postgraduate Division 2025 Zonal Ave., Los Angeles 33	S	II	Lec, O	20	Spring/59		I; 20 sessions 1 hr. weekly, Fridays	50
Principles and Clinical Uses of Radioisotopes	University of California Medical Center Second and Parnassus Ave., San Francisco	S	IC	Lab, BR, Sem, Lec, EPP	100	Arranged		C; 2 or 3 mo.	350
Radiology Physics and Medical Use of Isotopes	University of Colorado School of Medicine 4200 E. Ninth Ave., Denver 20	B Lim 20-25	II	PD, Sem, Lec		9/58	5/59	I; once weekly, Tuesdays for 9 mo.	10
The Clinical Uses of Radioisotopes	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 24	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, O, EPP	60	9/29/58 5/ 4/59	10/10/58	C; 10 days	200
Course in Radioisotope Techniques and Nuclear Medicine	Department of Nuclear Medicine, U.S. Naval Medical School National Naval Medical Center, Bethesda 14, Md.	S Lim 12	IC	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	850	9/ 4/58 1/19/59	12/19/58	C; 95 days	Unknown
Thyroid Disease and The Use of Radioactive Iodine	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General and Beth Israel Hospitals, Boston	S Lim 6	IC	Lab, PD, LC, Clin C, Lec	105	3/30/59	4/17/59	C; 18 days	300
Principles of Radioisotope Utilization	Director of the Summer Session Massachusetts Institute of Technology 77 Massachusetts Ave., Cambridge 39, Mass.	S Lim 100	IC	Lab, Lec	50	Summer/59		C; 10 days	Unknown
Medical Uses of Radioactive Isotopes	Queens General Hospital 82-68 164th St., Jamaica 32, N. Y.	S Training for AEC certification Lim 20	II	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, EPP	85	2/10/59	6/ 9/59	I; 17 sessions 5 hr. weekly, Tuesdays	250
Radiology PM 3a—Use of Radioactive Iodine	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S Lim 2	IC	Lab, PD, LC, Lec, O, AV	144	9/58 12/58 3/59	12/58	C; 40 days	300

Radiology PM 41—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	II	Lab, Lec, O, AV	90	9/15/58	4/ 6/59	I; 30 sessions 3 hr. weekly, Mondays	300
Radiology PM 40—Clinical Use of Radioactive Isotopes	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G Lim 15	IO	Lab, Lec, O, AV	140	6/ 1/59	6/26/59	C; 20 days	300
636-A. Radioactive Isotopes	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 2	PT	Lab, PD, LC, BR, Clin C, Sem, EPP	150	Arranged	1 mo. later		175
638-A. Radioactive Isotopes	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 1	II	Lab, PD, LC, BR, Clin C, Pan, EPP	102	10/ 8/58	5/27/59	I; 34 sessions 3 hr. weekly, Wednesdays	100
Basic Course in Radioisotope Techniques	Oak Ridge Institute of Nuclear Studies P. O. Box 117, Oak Ridge, Tenn.	B Lim 48	IO	Lab, PD, LC, Sem, Lec, O, AV, EPP	103	9/ 8/58	9/28/58	C; 20 days	25
Medical Use of Radioisotopes	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B and residents Lim 12	IO	Lab, PD, LC, Sem, Lec, EPP	100	5/ 4/59	5/29/59	C; 25 days	100
Clinical Application of Radioisotopes	School of Medicine, University of Puerto Rico San Juan 22, Puerto Rico	G Lim 3	IO	Lab, PD, LC, BR, Clin C, Sem, Lec, Pan, O, AV, EPP	400	8/15/58 10/15/58 12/15/58 2/15/59 4/15/59 6/15/59	11/15/58	C; 90 days	Nil

RADIOLOGY

(See also Cardiovascular Disease, Occupational Medicine, Radioisotopes)

Diagnostic Radiology	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G		Lab, Sem, Lec, Pan, O, AV	Undetermined	Spring/59		Unknown	Unknown
Diagnostic Radiology	University of California Medical Center Second and Parnassus Ave., San Francisco	S Lim 100	IO	Lec, Pan, O, AV	35	4/ 4/59	4/ 8/59	C; 5 days	75
Neuroroentgenology	Program Director, Connecticut Postgraduate Seminar in Psychiatry and Neurology, Connecticut State Hospital, Middletown, Conn.; course at Yale University School of Medicine, New Haven, Conn.	S Lim 30 to 40	II	Lec, O	8	9/22/58	10/13/58	I; 8 sessions 1 hr. weekly, Mondays	Nil
Radiology 302—Introduction to X-rays and Radioisotopes	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lec, O, AV	11	9/25/58	12/11/58	I; 11 sessions 1 hr. weekly, Thursdays	25
Radiology 303—X-ray Physics (Prerequisite Radiology 302)	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S	II	Lab, Lec, O, AV	20	1/ 8/59	3/12/59	I; 10 sessions 2 hr. weekly, Thursdays	40
Radiology 304—Radioactivity (Prerequisites Radiology 302 & 303)	Assistant Dean of Postgraduate Medical Education Yale University School of Medicine 333 Cedar St., New Haven, Conn.	S Lim	II	Lab, O, EPP	30	3/19/59	5/21/59	I; 10 sessions 3 hr. weekly, Thursdays	150
Course II—Clinical Radiology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 6	IO	Lab, PD, LC, BR, Clin C, Sem, Lec, O, EPP	50	Arranged	2 wk. later	C; 12 days	70
Course II—Clinical Radiology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 6	IO	Lab, PD, LC, BR, Clin C, Sem, Lec, O, EPP	100	Arranged By appointment	4 wk. later	C; 24 days	125
Course III—X-Ray Therapy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 3	PT	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, Pan, O, EPP	30 to 210	Arranged By appointment	1, 2, 4 or 8 wk. later	6 to 21 days	60 to 300
Course I—Diagnostic Radiology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 10	IO	Lab, PD, LC, BR, Clin C, Sem, Lec, O, EPP	68	9/22/58 12/ 1/58 3/ 2/59 4/27/59 6/15/59	10/ 3/58	C; 12 days	125

Key will be found on page 1954.

RADIOLOGY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Radium Therapy	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Clin C, Surg, O, EPP	30	6/ 1/59	6/ 5/59	C; 5 days	100
Radiation Physics	Northwestern University Medical School 303 E. Chicago Ave., Chicago 11	S Lim 60	II	Lec	36	1/ 5/59	4/13/59	I; 18 sessions 2 hr. weekly, Mondays	35 Practicing Physicians; 15 Residents
Radiation Therapy Seminar	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	S	II	Sem, Lec, O, AV	35	10/ 3/58	5/29/59	I; 35 sessions 1 hr. weekly, Fridays	5 per session
General Radiation Physics	Indiana University School of Medicine 1100 W. Michigan St., Indianapolis 7	S	II	Lec, O, AV	21	10/ 8/58	2/25/59	I; 21 sessions 1 hr. weekly, Wednesdays	100
Radiology	State University of Iowa College of Medicine University Hospitals, Iowa City	S	IO	PD, Lec, Pan, O, AV	9	10/10/58	10/11/58	C; 2 days	15
Radiological Physics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	II	Lec, O	20	1/11/59	3/15/59	I; 10 sessions 2 hr. weekly, Sundays	30
Radiology and Radioactive Isotopes	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	S	IC	Clin C, Lec, Pan, O, AV	21	2/ 9/59	2/11/59	C; 3 days	45
General Radiology I	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Peter Bent Brigham Hospital, Boston	S Lim 2	IC	Lab, PD, LC, Clin C, Sem	120 to 130 a mo.	Arranged		Arranged	150 a mo.
Diagnostic Radiology	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 45	IC	Lec, Pan, O, AV	20	4/ 6/59	4/10/59	C; 5 days	50
Pediatric Radiology for Radiologists	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Sem, Lec, Pan, O, AV	33	11/ 3/58	11/ 8/58	C; 6 days	100
Radiology for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, O, AV	15	4/ 6/59	4/ 8/59	C; 3 days	40
Modern Concepts in Roentgenology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 30	II	Lec, AV	15	Unknown		I; 10 sessions 1½ hr. each	50
Use and Interpretation of Diagnostic X-Ray	University of Buffalo School of Medicine 3435 Main St., Buffalo	G	IO	Sem, Lec, Pan, O	14	9/17/58	9/18/58	C; 2 days	30
X-Ray Diagnosis	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 20	II	Lec	15	10/ 1/58	1/ 7/59	I; 15 sessions 1 hr. weekly, Wednesdays	30
Operative Use of Radium and Radioactive Sources	Queens General Hospital 82-68 164th St., Jamaica 32, N. Y.	S Lim 8	II	Lab, PD, LC, Clin C, Sem, Surg, Lec, Pan, O	24	11/ 1/58	12/20/58	I; 8 sessions 3 hr. weekly, Saturdays	100
Roentgen Diagnosis in Gastroenterology	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Beth-El Hospital, Brooklyn, N.Y.	G Lim 30	II	Lec, AV	8	10/58	12/58	I; 8 sessions 1 hr. weekly, Tuesdays	20
X-Ray Diagnosis of Chest Diseases, Heart and Lung	Beth-El Hospital Linden Blvd. & Rockaway Parkway, Brooklyn, N. Y.	G Lim 12	II	Lec, AV	12	4/17/59	5/29/59	I; 2 hr. weekly, Thursdays	20
Radiology PM 51—Radiotherapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	IC	Lab, LC, Lec, EPP		Unknown		C; 6 or 12 mo. full time	300 for 6 mo.; 600 for 12 mo.
Radiology PM 31—Chest	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IO	Lec, O, AV	10½	9/30/58 3/16/59	10/ 7/58	C; 7 days	50

Radiology PM 30—Roentgenographic Interpretation of the Diseases of Bones and Joints	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Hospital for Joint Diseases, New York 35	G	II	Lec, O, AV	24	10/ 1/58	12/17/58	I; 12 sessions 2 hr. weekly, Wednesdays	150
Radiology PM 31—Chest, Differential Diagnosis	Columbia University College of Physicians and Surgeons *630 W. 168th St., New York 32;* *course at Mount Sinai Hospital, New York 29*	G Lim 3	II	PD, LC	15	10/18/58 3/30/59	12/15/58	I; 10 sessions 1½ hr. weekly, Mondays	50
Radiology PM 1—Radiological Physics	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Columbia-Presbyterian Medical Center, New York 32	S	II	Lec, O, AV	36	1/13/59	5/15/59	I; 36 sessions 1 hr. twice weekly, Tuesdays, Thursdays	50
Radiology PM 32—Gastrointestinal Tract	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	G	IC	Lec, O, AV	10	3/ 2/59	3/13/59	C; 10 days	50
Radiology PM 33—Radium Therapy	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	S	II	Lec, O, AV	12	5/19/59	6/23/59	I; 6 sessions 2 hr. weekly, Tuesdays	50
X-Ray Diagnosis of Chest Diseases	Joint Committee on Post-Graduate Education 1313 Bedford Ave., Brooklyn, N. Y.; course at Beth-El Hospital, Brooklyn, N. Y.	G Lim 30	II	Lec, AV	8	4/15/59	6/10/59	I; 8 sessions 1 hr. weekly, Wednesdays	20
Roentgen Interpretation	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	PD, Lec, O	480	10/ 1/58 4/ 1/59	12/31/58	C; 72 days	300
657-A. Radiological Aspects of Medicolegal Medicine	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 150	II	Sem, Lec, Pan, O, AV	18	9/23/58	12/ 9/58	I; 12 sessions 1½ hr. weekly, Tuesdays	35
651-A. Diagnostic Radiology For General Practitioners	*New York University Post-Graduate* Medical School 550 First Ave., New York 16	*G* Lim 50	*II*	Lec	60	9/24/58	4/29/59	I; 30 sessions 2 hr. weekly, Wednesdays	125
655-A. Clinical Radiation Therapy	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 2	II	PD, LC, BR, Clin C, Sem, Lec, O	54	10/ 1/58	1/28/59	I; 18 sessions 3 hr. weekly, Wednesdays	100
651-A. Radiobiology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	II	Sem, Lec	34	2/ 4/59	5/27/59	I; 17 sessions 2 hr. weekly, Wednesdays	75
Operative Radium Therapy—Operative Use of Radium and Radioactive Sources	Queens General Hospital 82-68 164th St., Jamaica 32, N. Y.	S Lim 8	II	Lab, PD, LC, Clin C, Sem, Surg, Lec, Pan, O	24	11/ 1/58	12/20/58	I; 8 sessions 3 hr. weekly, Saturdays	100
Instructional Course	The Radiological Society of North America, Inc. 713 E. Genesee St., Syracuse, N. Y.; course at Palmer House, Chicago	S Lim 50	IC	Lab, PD, Lec, Pan, O	81½	11/16/58	11/21/58	C; 6 days	15
Physics of Radiology	The Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland	S Lim 50	II	Sem, Lec, O	34	12/ 4/58	4/ 9/59	Unknown	30
Practical Course in Radiological Physics	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B and residents Lim 6	IC	Lab, Sem, Lec, EPP	200	1/ 5/59	2/27/59	C; 40 days	200

SURGERY

(See also Anatomy, Basic Sciences, Cardiovascular Disease, Endoscopy, General Practice, Gynecology, Internal Medicine, Malignant Disease, Neurology, Pathology, Pulmonary Disease, Radioisotopes)

Clinical Sciences	College of Medical Evangelists 1720 Brooklyn Ave., Los Angeles 33	G Lim 20	IO	Lab, BR, Surg, Sem, Lec, Pan, Dem	1400	9/ 8/58	6/ 5/59	C; 175 days	800
Minor Surgery	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 80	IC	Lab, Sem, Lec, Pan, O, AV, EPP	12	9/ 5/58	9/ 6/58	C; 2 days	65 Lecture and Lab. 40 Lecture only
Removal of Foreign Bodies from Trachea and Bronchi	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 12	IO	Lab, Surg, Lec, O, AV, EPP	10	11/ 8/58	11/ 9/58	C; 2 days	100

Key will be found on page 1954.

SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Surgery of Trauma	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G	IC	Sem, Lec, Pan, O, AV		Fall/58		Unknown	Unknown
Techniques of Surgery	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 24	G Lim 14	IC	Lab, Sem, Lec, O, AV, EPP	30	7/59		C; 5 days	500
Course in a Phase of Surgery	California Medical Assoc. 2975 Wilshire Blvd., Los Angeles; course at Stanford University, San Francisco	S Lim 60	IC	Surg, Lec, Pan, O	12	2/23/59	2/25/59	C; 3 days	25
Plastic Surgery	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	Lec, Pan, O, AV	7	11/13/58	11/13/58	C; 1 day	20
Hand Surgery	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	Lec, Pan, O, AV	7	11/14/58	11/14/58	C; 1 day	20
Course in General Surgery	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IC	PD, Surg, Lec, Pan, O, AV, TV	35	4/59		C; 5 days	75
A Series of Postgraduate Surgical Programs	U. S. Veterans Administration Hospital (Fort Miley) 42nd Ave. and Clement St., San Francisco	G Lim 300	II	Lab, PD, LC, Sem, Lec, Pan, O	12	10/14/58	11/18/58	I; 6 sessions 2 hr. weekly, Tuesdays	15 AAGP Mem.; 300 Non-Mem.
Oral Surgery	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Institute of Research, Washington 12, D. C.	G (and Dentists) Restricted to members of the Federal Services	IC	PD, Clin C, Sem, Surg, Lec, O, AV, TV	40 to 45	1/ 5/59	1/ 9/ 59	C; 5 days	Nil
Surgery in Acute Trauma	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Brooke Army Medical Center, Ft. Sam Houston, Tex.	G Lim 100	IC	Clin C, Sem, Lec	24	3/ 9/59	3/11/59	C; 3 days	Nil
Physiological Considerations in Surgery	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Walter Reed Army Hospital, Washington 12, D. C.	S Restricted to members of the Federal Services Lim 50	IC	PD, Clin C, Sem, Lec, O, TV	44	4/ 6/59	4/11/59	C; 6 days	Nil
Surgery in Acute Trauma	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at William Beaumont Army Hospital, El Paso, Tex.	G Lim 100	IC	Lec		4/ 7/59	4/ 9/59	C; 3 days	Nil
Oral Surgery	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Letterman Army Hospital, San Francisco	G (and dentists) Restricted to members of the Federal Services Lim 30	IC	Lab, LC, Sem, Lec, Pan, O, AV	40	4/20/59	4/24/59	C; 5 days	Nil
Seminar on Selected Topics in Surgery	University of Florida, College of Medicine Division of Postgraduate Education J. Hillis Miller Health Center Gainesville, Fla.	B	IC	PD, Clin C, Sem, Lec, Pan, O, AV	15	11/58		C; 2½ days	25
Professor Pro Tempore Surgery	Mt. Sinai Hospital of Greater Miami 4300 Alton Rd., Miami Beach 40, Fla.	S Lim 100	IC	PD, LC, BR, Clin C, Surg, Lec, Pan, O, AV	30	3/23/59	3/28/59	C; 6 days	25
Esophageal Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 16	IC	PD, LC, BR, Surg, Lec, O, AV	25	9/15/58 6/15/59	9/19/58	C; 5 days	150
Course I in Surgical Technic	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Surg, Lec, O, AV, EPP	90	9/15/58 9/29/58 10/27/58 11/10/58 12/ 1/58 2/ 2/59 2/16/59 3/16/59 4/20/59 5/11/59 6/15/59 7/20/59 8/17/59	9/27/58	C; 12 days	250

Surgery of Colon and Rectum	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	45	9/22/58 10/27/58 12/ 1/58 3/ 2/59 4/ 6/59 5/ 4/59 6/ 1/59	9/26/58	C; 5 days	125
Thoracic Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 18	IC	Lab, PD, LC, BR, Surg, Lec, O, AV	30	9/22/58 6/22/59	9/27/58	C; 6 days	125
Annual Postgraduate Course of the United States Section of the International College of Surgeons	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 50	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	78	10/13/58 7/ 6/59	10/25/58	C; 11 days	150
Basic Principles in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	85	10/13/58 4/ 6/59 7/ 6/59	10/24/58	C; 12 days	150
Blood Vessel Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	35	10/20/58 3/ 2/59	10/24/58	C; 5 days	125
One Week Course in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	PD, LC, BR, Surg, Lec, O, AV	25	10/27/58 2/ 9/59 5/11/59	10/31/58	C; 5 days	150
Gallbladder Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	PD, LC, BR, Surg, Lec, O, AV	10	11/ 3/58 3/30/59 6/ 1/59	11/ 5/58	C; 3 days	80
Surgery of Hernia	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 16	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	13	11/ 6/58 4/ 2/59 6/ 4/59	11/ 8/58	C; 3 days	80
General Surgery for the Specialist	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	S Lim 40	IC	Lab, PD, LC, BR, Clin C, Sem, Surg, Lec, O, AV	80	11/10/58 4/ 6/59	11/22/58	C; 12 days	250
Two-Week Course in General Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 18	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	70	11/10/58 5/ 4/59	11/22/58	C; 12 days	250
Breast and Thyroid Surgery	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 18	IC	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV	34	5/ 4/59	5/ 9/59	C; 6 days	150
General Surgery	Chicago Medical Society 86 E. Randolph St., Chicago; course at Hamilton Hotel, Chicago	G Lim 100	IC	Lec, Pan, O	20½	11/ 3/58	11/ 7/58	C; 5 days	75
General Surgery	State University of Iowa College of Medicine University Hospitals, Iowa City	G	IC	PD, BR, Lec, Pan, O, AV	18	12/ 9/58	12/11/58	C; 3 days	30
Surgery—Operative Clinics	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G Lim 25	II	Surg, Lec, O, AV, TV	32	11/19/58	3/18/59 (excluding December)	I; 4 sessions 8 hr. once mo., Wednesdays	50
Neurology and Neurosurgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks	G	IC	PD, Lec, Pan, O, AV	14	2/25/59	2/26/59	C; 2 days	30
General Surgery	University of Kansas Medical Center 39th and Rainbow Blvd., Kansas City, Ks.	G	IC	PD, BR, Sem, Lec, Pan, O, AV	28	5/18/59	5/21/59	C; 4 days	60
Surgery of Trauma	Tulane University School of Medicine 1430 Tulane Ave., New Orleans	B Lim 50	IC	PD, Sem, Lec, Pan, O	20	2/26/59	2/28/59	C; 2½ days	25
General Surgery I	Harvard Medical School, Courses for Graduates 25 Shattuck St., Boston 15; course at Massachusetts General Hospital, Boston	G Lim 25	IC	PD, LC, BR, Clin C, Lec	110	10/14/58 6/ 1/59	10/31/58	C; 15 days	250
Clinical Exercises for Practitioners	University of Michigan Medical School Department of Postgraduate Medicine University Hospital, Ann Arbor, Mich.	G Lim 50	II	PD, LC, Clin C, Lec, Pan	80	10/ 8/58	2/25/59	I; 20 sessions 4 hr. weekly, Wednesdays	65
Surgery for Surgeons	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	S	IC	Surg, Lec, O, AV	15	1/22/59	1/24/59	C; 3 days	40
Emergency Surgery for General Physicians	Continuation Medical Education 1342 Mayo Memorial University of Minnesota, Minneapolis 14	G	IC	Lec, Pan, O, AV	15	4/ 2/59	4/ 4/59	C; 3 days	40
In Hospital Review in Surgery	Office of Postgraduate Affairs University of Nebraska College of Medicine 42nd and Dewey Sts., Omaha 5	G Lim 5 members Neb. A.G.P.	PT	PD, LC, BR, Clin C, Sem, Surg, O, AV, EPP	40	Autumn/58		5½ days	50

Key will be found on page 1954.

SURGERY—Continued

Title of Course	Location	Designed For	Type	Methods of Instruction	Total Hours	Starting Date	Ending Date	Time Arrangement	Fee
Recent Advances in Surgery	St. Michael's Hospital 306 High St., Newark, N. J.	G Lim 50	II	PD, Clin C, Lec, O, AV	18	9/58	2/59	I; 9 sessions 2 hr. mo., Saturdays	25
Clinical Surgery	Seton Hall College of Medicine and Surgery, Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 30	II	PD, Clin C, Lec, O, AV	15	Unknown		I; 10 sessions 1½ hr. weekly, Wednesdays	50
Experimental Vascular Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 15	II	Lab, O, AV, EPP	33	9/20/58	10/29/58	I; 11 sessions 3 hr. weekly, Saturdays	225
Surgical Techniques and Principles of Abdominal Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 20	II	Lab, Lec, O	9	10/14/58	12/19/58	I; 6 sessions 1½ hr. weekly, Fridays	100
Experimental Gastrointestinal Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	G Lim 12	II	Lab, O, EPP	18	12/ 6/58	1/24/59	I; 6 sessions 3 hr. weekly	125
Surgical Physiology	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Martland Medical Center, Newark, N. J.	S Lim 30	II	Lec, O, AV	7½	1/ 7/59	2/ 4/59	I; 5 sessions 1½ hr. weekly, Wednesdays	35
Modern Concepts in Surgery	Seton Hall College of Medicine and Dentistry Department of Postgraduate Medical Education 31 Clinton St., Newark, N. J.; course at Monmouth Memorial Hospital, Long Branch, N. J.	G Lim 50	II	Lec, O, AV	15	3/10/59	5/12/59	I; 10 sessions 1½ hr. weekly, Tuesdays	50
Recent Advances in Surgery	Albany Medical College 47 New Scotland Ave., Albany 8, N. Y.	G	IC	PD, LC, Clin C, Sem, Pan, O, AV	6	2/12/59	2/12/59	C; 1 day	12
Management of the Cardiac Surgical Patient	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G	II	Lec	6	10/ 1/58	10/22/58	I; 4 sessions 1½ hr. weekly, Wednesdays	10
Office Surgery and Proctology	Nassau Academy of Medicine, Inc. 1200 Stewart Ave., Garden City, N. Y.; course at Meadowbrook Hospital, East Meadow, N. Y.	G Lim 8	II	LC, Lec	20	10/10/58	12/12/58	I; 20 sessions 1 hr. twice weekly, Wednesdays, Fridays	35
Medicine PM 65A-Peripheral Vascular Surgery	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Montefiore Hospital, New York 67	G Lim 15	II	PD, Sem, Lec, O, AV	51	11/12/58	3/18/59	I; 17 sessions 3 hr. weekly, Wednesdays	150
Surgery PM 31—Minor Surgery	Columbia University College of Physicians and Surgeons 630 W. 168th St., New York 32; course at Mount Sinai Hospital, New York 29	B Lim 8	IC	PD, LC, Lec, O, AV	24	12/ 1/58	12/ 3/58	C; 3 days	75
Thoracic Surgery (Cadaver demonstration)	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 8	II	LC, BR, Lec, O, AV, EPP	12	Arranged		I; 6 sessions 2 hrs. thrice weekly, Mondays, Wednesdays, Fridays	200
Vascular Surgery (Cadaver demonstrations)	New York Polyclinic Hospital 315 W. 50th St., New York 19	G Lim 10	II	Lec	16	Arranged		I; 2 hr. each on 8 Thursdays	200

Combined Surgical Course including Cadaver Surgery and Gynecology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 20	IC	Lab, PD, LC, BR, Clin C, Lec, O, AV	420	10/ 1/58 4/ 1/59	11/30/58	C: 48 days	350
668-A. Recent Advances in Surgery	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	PD, LC, Clin C, Sem, Lec, Pan	78	9/ 8/58	9/20/58	C: 11 days	200
660-A. Modern Concepts of the Etiology, Pathologic Physiology and Therapy of Diseases with Surgical Implications	New York University Post-Graduate Medical School 550 First Ave., New York 16	G	H	PD, Clin C, Lec, Pan, O, AV	111	9/11/58	6/18/59	I: 37 sessions 3 hr. weekly, Thursdays	300
551-A. The Intervertebral Disc	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 6	IC	PD, BR, Clin C, Surg, AV	14	10/ 9/58	10/10/58	C: 2 days	50
553-A. Problems in Practice Requiring Neurosurgical Investigation	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, BR, Clin C, Surg, AV	35	10/13/58 4/27/59 6/22/59	10/17/58	C: 5 days	125
661-A. Review of General Surgery	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	Lab, PD, LC, Clin C, Sem, Lec, Pan	176	10/20/58	11/15/58	C: 24 days	300
552-A. Diagnosis and Treatment of Peripheral Nerve Injuries	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 8	IC	Lab, PD, Surg, Lec, EPP	14	1/ 8/59	1/ 9/59	C: 2 days	50
662-A. Basic Problems in Cancer Therapy (For Surgeons)	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 20	IC	Lab, PD, Clin C, Sem, Lec, Pan, O, AV	88	1/19/59	1/31/59	C: 12 days	200
667-A. Surgery of the Hand	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 20	IC	PD, LC, Clin C, Sem, Surg, Lec, AV	42	3/16/59	3/21/59	C: 6 days	100
Recent Advances in Surgery	The Frank E. Bunts Educational Institute 2020 E. 93rd St., Cleveland	B Lim 125	IC	LC, Sem, Lec, Pan, O, AV	14	12/10/58	12/11/58	C: 2 days	25
Bronchology, Esophagology and Laryngeal Surgery	University of Pennsylvania Graduate School of Medicine 237 Medical Lab. Bldg., Philadelphia	S Lim 20	IC	PD, LC, Lec, O, AV		6/ 2/59	6/14/59	C: 14 days	250
A Postgraduate Review in Surgery	Vanderbilt University School of Medicine and Hospital 21st Ave. South, Nashville, Tenn.	G	IC	PD, LC, Clin C, Lec, Pan, O	6	Spring/59	Spring/59	C: 1 day	15
Surgery	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive, Houston 25, Tex; course at Turner Home, El Paso, Tex	G	IC	Lec, O, AV	7	12/ 6/58	12/ 6/58	C: 1 day	10

UROLOGY

(See also Anatomy, Infertility)

Office Urology	Department of Continuing Education in Medicine and Health Sciences University of California Medical Center Los Angeles 21	G	IO	PD, Lec, O, AV	6	2/59		C: 1 day	Unknown
Urology	University of California Medical Center Second and Parnassus Ave., San Francisco	G Lim 100	IO	Lec, Pan, O, AV	7	11/ 7/58	11/ 7/58	C: 1 day	20
James C. Kimbrough Urological Seminar	Department of the Army Office of the Surgeon General Personnel and Training Division Washington 25, D. C.; course at Brooke Army Medical Center, Ft. Sam Houston, Tex.	S Lim 100	IC	PD, BR, Lec	24	11/ 3/58	11/ 5/58	C; 3 days	Nil
Urology	Cook County Graduate School of Medicine 707 S. Wood St., Chicago 12	G Lim 12	IO	Lab, PD, LC, BR, Clin C, Surg, Lec, O, AV, EPP	80	10/13/58 3/30/59	10/25/58	C; 12 days	225
Urology Conference	State University of Iowa College of Medicine University Hospitals, Iowa City	S	IO	PD, BR, Surg, Lec, Pan, O, AV	9	9/26/58	9/27/58	C; 2 days	15
Instrumental and Operative Urology	New York Polyclinic Hospital 345 W. 50th St., New York 19	G Lim 12	IC	Lab, PD, LC, BR, Clin C, Lec, Pan, O, AV	64	10/ 1/58 4/ 1/59	10/31/58	C; 24 days	250
674-A. Refresher Course in Basic Urology	New York University Post-Graduate Medical School 550 First Ave., New York 16	G Lim 12	IC	Lab, Lec, O, EPP	35	1/12/59	1/16/59	C: 5 days	75
671-A. Advanced Course in Urology	New York University Post-Graduate Medical School 550 First Ave., New York 16	S Lim 10	IO	Lab, PD, BR, Clin C, Sem, Lec, O, EPP	70	5/11/59	5/22/59	C: 10 days	200
Trends in Urology	University of Texas Postgraduate School of Medicine 1400 Outer Belt Drive Houston 25, Tex.; course at The University of Texas M.D. Anderson Hospital, Houston, Tex.	B Lim 270	IO	Lec, Pan, TV	15	2/19/59	2/21/59	C: 3 days	35

Key will be found on page 1954.

MEDICINE AND THE LAW

TAX DEDUCTION OF EXPENSES OF POSTGRADUATE EDUCATION

The full text of the Internal Revenue Service regulation governing tax deduction of expenses of postgraduate education is herewith reproduced in full.

§ 1.162-5. Expenses for education.—(a) Expenditures made by a taxpayer for his education are deductible if they are for education (including research activities) undertaken primarily for the purpose of:

(1) Maintaining or improving skills required by the taxpayer in his employment or other trade or business, or

(2) Meeting the express requirements of a taxpayer's employer, or the requirements of applicable law or regulations, imposed as a condition to the retention by the taxpayer of his salary, status or employment.

Whether or not education is of the type referred to in subparagraph (1) of this paragraph shall be determined upon the basis of all the facts of each case. If it is customary for other established members of the taxpayer's trade or business to undertake such education, the taxpayer will ordinarily be considered to have undertaken this education for the purpose described in subparagraph (1) of this paragraph. Expenditures for education of the type described in subparagraph (2) of this paragraph are deductible under subparagraph (2) only to the extent that they are for the minimum education required by the taxpayer's employer, or by applicable law or regulations, as a condition to the retention of the taxpayer's salary, status, or employment. Expenditures for education other than those so required may be deductible under subparagraph (1) of this paragraph if the education meets the qualifications of subparagraph (1). A taxpayer is considered to have made expenditures for education to meet the express requirements of his employer only if the requirement is imposed primarily for a bona fide business purpose of the taxpayer's employer and not primarily for the taxpayer's benefit. Except as provided in the last sentence of paragraph (b) of this section, in the case of teachers, a written statement from an authorized official or school officer to the effect that the education was required as a condition to the retention of the taxpayer's salary, status, or employment will be accepted for the purpose of meeting the requirements of this paragraph.

(b) Expenditures made by a taxpayer for his education are not deductible if they are for education undertaken primarily for the purpose of obtaining a new position or substantial advancement in position, or primarily for the purpose of fulfilling the general educational aspirations or other personal purposes of the taxpayer. The fact that the education undertaken meets express requirements for the new position or substantial advancement in position will be an important factor indicating that the education is undertaken primarily for the purpose of obtaining such position or advancement, unless such education is required as a condition to the retention by the taxpayer of his present employment. In any event, if education is required of the taxpayer in order to meet the minimum requirements for qualification or establishment in his intended trade or business or specialty therein, the expense of such education is personal in nature and therefore is not deductible.

(c) In general, a taxpayer's expenditures for travel (including travel while on sabbatical leave) as a form of education shall be considered as primarily personal in nature and therefore not deductible.

(d) If a taxpayer travels away from home primarily to obtain education the expenses of which are deductible under this section, his expenditures for travel, meals, and lodging while away from home are deductible. However, if as an incident of such trip the taxpayer engages in some personal activity such as sightseeing, social visiting or entertaining, or other recreation, the portion of the expenses attributable to such personal activity constitutes nondeductible personal or living expenses and is not allowable as a deduction. If the taxpayer's travel away from home is primarily personal, the taxpayer's expenditures for travel, meals, and lodging (other than meals and lodging during the time spent in participating in deductible educational pursuits) are not deductible. Whether a particular trip is primarily personal or primarily to obtain education the expenses of which are deductible under this section depends upon all the facts and circumstances of each case. An important factor to be taken into consideration in making the determination is the relative amount of time devoted to personal activity as compared with the time devoted to educational pursuits. Expenses in the nature of commuters' fares are not deductible.

(e) The provisions of this section may be illustrated by the following examples:

Example (1). A is employed by an accounting firm. In order to become a certified public accountant he takes courses in accounting. Since the education was undertaken prior to the time A became qualified in his chosen profession as a certified public accountant, A's expenditures for such courses and expenses for any transportation, meals, and lodging while away from home are not deductible.

Example (2). B, a general practitioner of medicine, takes a course of study in order to become a specialist in pediatrics. C, a general practitioner of medicine, takes a 2-week course reviewing developments in several specialized fields, including pediatrics, for the purpose of carrying on his general practice. B's expenses are not deductible because the course of study qualified him for a specialty within his trade or business. C's expenses for his education and any transportation, meals, and lodging while away from home are deductible because they were undertaken primarily to improve skills required by him in his trade or business.

Example (3). D is required by his employer (or by State law) either to read a list of books or to take certain courses giving six hours academic credit every two years in order to retain his position as a teacher. D fulfills the requirement by taking the courses and thereby receives an automatic increase in salary in his present position and salary schedule. Also, as the result of taking the prescribed courses, at the end of ten years, D receives a master's degree and becomes automatically eligible for an additional salary increase. Since D's purpose in taking the courses was primarily to fulfill the educational requirement of his employer, his expenses for such education and transportation, meals, and lodging while away from home are deductible.

Example (4). The facts are the same as in example (3) except that, due solely to a shortage of qualified teachers, D's employer does not enforce the prescribed educational requirements in that other teachers who do not fulfill those requirements are retained in their positions. D's expenses are nevertheless deductible.

Example (5). E, a high school teacher of physics, in order to improve skills required by him and thus improve his effectiveness as such a teacher, takes summer school courses in nuclear physics and educational methods. E's expenses for such courses are deductible.

Example (6). F takes summer school courses in order to improve skills required by him in his employment as a teacher. As a result of taking such courses F receives an in-grade increase in salary in his present position pursuant to a salary schedule established by the school system for which he works. F's expenditures for such courses are deductible.

Example (7). G, a graduate student at a university, plans to become a university professor. In order to qualify as a regular faculty member, G must obtain a graduate degree. While taking the required graduate courses, G is engaged in teaching at the university. G's expenses therefor are not deductible since he has not completed the education required to become qualified as a regular faculty member at the time he takes such courses.

Example (8). H, a self-employed tax consultant, decides to take a 1-week course in taxation, which is offered in City X, 500 miles away from his home. His primary purpose in going to X is to take the course, but he also takes a side trip to City Y (50 miles from X) for one day, takes a sightseeing trip while in X, and entertains some personal friends. H's transportation expenses to City X and return to his home are deductible but his transportation expenses to City Y are not deductible. H's expenses for meals and lodging while away from home will be allocated between his educational pursuits and his personal activities. Those expenses which are entirely personal, such as sightseeing and entertaining friends, are not deductible to any extent.

Example (9). The facts are the same as in example (8) except that H's primary purpose in going to City X is to take a vacation. This purpose is indicated by several factors, one of which is the fact that he spends only one week attending the tax course and devotes five weeks entirely to personal activities. None of H's transportation expenses are deductible and his expenses for meals and lodging while away from home are not deductible to the extent attributable to personal activities. His expenses for meals and lodging allocable to the week attending the tax course are, however, deductible. [Reg. § 1.162-5.]

MEDICAL NEWS

ALABAMA

Land Purchased by Medical Center.—Expansion of the University of Alabama Medical Center, Birmingham, was revealed in formal ceremonies in the University Hospital Auditorium June 9 with transfer of a deed to a 10½-block area. Mr. Hill Ferguson, chairman pro-tem of the university board of trustees, delivered a check for $2,654,990 to the Housing Authority of the Birmingham District in return for the deed, culminating seven years of work. The acquisition of the 10½-block area was made possible by the passage of Amendment No. 4 by the voters of Alabama in 1957. Expansion projects to be started soon in the Medical Center are student housing quarters and a 2½-million-dollar nurses' residency. Already being constructed is a 2-million-dollar six-story research building.

Hospital News.—The Susie Parker Stringfellow Memorial Hospital, a $365,000 one-story building with equipment, which was dedicated in Anniston in January, replaces a private residence operated at the same location for many years as a tuberculosis sanatorium. The hospital was financed through Mrs. Stringfellow's endowment in conjunction with funds from the Hill-Burton Act.——The second floor of the new addition to the Jackson Hospital and Clinic, Montgomery, was recently dedicated to the late Dr. John Randolph Penton Sr., former president of the hospital and clinic. A portrait of Dr. Penton hangs in the hall of the second floor and the section will be called the Penton section of the hospital.

CALIFORNIA

Announce Awards for Heart Research.—Awards totaling $165,770.40 to support heart research at local medical schools and hospitals have been announced by the Los Angeles County Heart Association. The 23 awards include a $50,000 grant in support of the Heart Association's Cardiovascular Research Laboratory at the University of Southern California School of Medicine, Los Angeles, in addition to funds for one established investigator, four research fellowships, and 17 grants-in-aid to institutions. Dr. Mitchel D. Covel, research committee chairman, said the awards were made possible by voluntary gifts to the 1958 Heart Fund. The funds will support several new studies and continue others during the next 12 months.

Dr. Ward Appointed Department Chairman.—Appointment of Dr. Robert Ward as physician-in-chief and director of research at Childrens Hospital and professor and chairman of the department of pediatrics at the University of Southern California School of Medicine, Los Angeles, has been announced. Dr. Ward, formerly professor of pediatrics at New York University, New York City, succeeds Dr. Merl J. Carson, now on sabbatical leave to take advanced training at the Neurological Institute, Queen's Square, London, England. Dr. Ward has served as president and secretary of the Society for Pediatric Research and is a fellow of the American Academy of Pediatrics and a member of the Commission on Viral Infections, Armed Forces Epidemiological Board.

Medical Care Center in Hemet.—The Friendly Hills Fellowship, a nonprofit foundation established "to provide a center where doctors and ministers may refer people not only in need of medical care, but also seeking peace of mind and a greater degree of spiritual awareness," has announced that its facilities are now available. These include the 560-acre Friendly Hills Ranch, two staff houses, and Meadowlark Farm, which is a 30-acre estate with a central house, two guest cottages, a staff house, stables, a swimming pool, and a picnic house. Financing of the foundation is partially from the resident guests and from contributions. President of the fellowship is Dr. Evarts G. Loomis Jr., who, in addition to his general practice in the Hemet community, began the Friendly Hills Ranch five years ago. Dr. David F. Meens, formerly engaged in a similar program in Colorado, is also on the staff. For information write Dr. Loomis at the Friendly Hills Fellowship, Route 1, Box 397, Hemet, Calif.

DISTRICT OF COLUMBIA

Narcotics Violation.—Dr. Norbert P. Gillem, 1733 U Street, N. W., Washington, D. C., was arrested on July 23, 1957, by officers of the Metropolitan Police Department for violations of the narcotic law. On April 14, 1958, he pleaded guilty in Federal Court, Washington, D. C., to violation of the District of Columbia Uniform Narcotic Drug Act, and on May 2, 1958, was sentenced to six months imprisonment by Judge Bolitha J. Laws.

Personal.—Theodore Koppanyi, Ph.D., chairman, department of pharmacology, Georgetown University Medical Center, has received an award to participate in the International Educational Exchange

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Program under the Fulbright Act. He will lecture in pharmacology at the Hebrew University, Jerusalem, Israel, during the 1958-1959 academic year.——Dr. John C. Rose, associate professor of medicine, Georgetown University Medical Center, has been appointed acting chairman of the department of physiology effective July 1. He succeeds Charles F. Morgan, Ph.D., who resigned to become research professor of pharmacology.

Dr. Peabody Honored by Chest Physicians.—Dr. J. Winthrop Peabody, past-president of the American College of Chest Physicians, was presented with the college medal and certificate of award "for meritorious achievement in the specialty of disease of the chest" at the annual meeting June 21. The award was given in recognition of Dr. Peabody's "unselfish devotion to the aims and ideals of the College since its foundation, but particularly to the advancement of postgraduate medical education." Since its inception in 1946 he has served as chairman of the Council on Postgraduate Medical Education of the college. In 1951 he was awarded the Vicennial Medal "for long and distinguished service." He was elected emeritus professor at Georgetown in 1957, marking 36 years of continuous teaching in the university. In 1953 he was awarded a certificate of merit by the Department of Public Health for 37 years of service. He served as first Chairman of the Section on Diseases of the Chest, American Medical Association, which was organized in 1952.

FLORIDA

Plan New Hospital in Miami.—A group of 75 members of the Dade County Medical Association are proceeding with plans to build a 200-bed hospital, the Cedars of Lebanon, in Miami. This is to be a nonprofit, nonsectarian institution and is planned to include air-conditioning and modern facilities for private patient care. The hospital will be located on the old Country Club grounds adjoining the projected Baptist Hospital, close enough to Jackson Memorial to form a part of the over-all patient-care facilities in the University of Miami School of Medicine environs. Initial funds for construction are being raised by the sale of interest-bearing bonds, part of which have been guaranteed by the founding group. The deficit of hospital beds is aggravated by the increases in population, reportedly at the rate of 20 additional beds per month.

ILLINOIS

Student Health Center at Northwestern.—A new health center for students of Northwestern University will be started early in 1959 on the Evanston campus, Dr. J. Roscoe Miller, president, has announced. The project, to be known as Searle Health Center, will cost $800,000, which will be provided as a gift to the University by John G. Searle, of Winnetka, a vice-president of the university's board of trustees and president of G. D. Searle & Co., Chicago medical research and pharmaceutical manufacturing organization. Searle Health Center will be a part of the university's 138½-million-dollar long-range development plan. Construction is scheduled to begin in March, 1959, and completion and dedication are scheduled for January, 1960. Preliminary plans provide for a two-story building with clinic facilities on the ground floor and an infirmary on the top floor.

Chicago

Service for Chronically Ill Persons.—The Central Service for the Chronically Ill of The Institute of Medicine of Chicago was established in 1943 to help patients who need continuing care, either at home or in a nursing home, get information about the services available for their care. The organization is supported by the Chicago Medical Society, the Community Fund of Chicago, the Chicago Community Trust, foundations, and individuals. The service provides information on nursing services, special equipment, therapy, and costs for home care, and management, treatment, feeding and care, and costs for nursing home care. Dr. Henry L. Schmitz is president of the board of directors for the service. For information write The Central Service for the Chronically Ill, The Institute of Medicine of Chicago, 86 E. Randolph St., Chicago 1; phone, FI 6-2677.

Hospital News.—John N. Hatfield, director of Passavant hospital, has been named recipient of the 1958 distinguished service award of the American Hospital Association. The award, given for "outstanding leadership in hospital administration," will be presented Aug. 20 at the association's annual convention. Mr. Hatfield has been director of Passavant hospital since 1952.——New medical staff officers installed at Mercy Hospital May 24 include chief of staff, Dr. Joseph E. Laibe; vice-president, Dr. Cornelius M. Annan; and secretary-treasurer, Dr. William F. Cernock. Nominated to serve on the executive board of the hospital are Dr. Arkell M. Vaughn and Dr. Harold C. Voris.

Dr. Moseley to Head Department of Radiology.—Dr. Robert David Moseley Jr. has been named professor and chairman of the department of radiology, University of Chicago, effective July 1, succeeding Dr. Paul C. Hodges, who has reached retirement age. Dr. Moseley came to the University of Chicago in 1949 as an assistant resident in radiology. In 1950 he was assigned by the university to the Los Alamos Special Research Project, and in 1951 he became a staff member, Radiobiological Research Group, at the Los Alamos Scientific Laboratory of the University of California at Los Alamos, N. M. He returned to the University of Chicago as an instructor in the department of radiology in 1954; he became assistant professor and clinical fellow of the American Cancer Society in 1955 and associate professor in 1957. In January, 1958, he was appointed to the staff of the Argonne Cancer Research Hospital.

Personal.—Honorary membership in the Royal College of Surgeons in London has been awarded to Dr. Warren H. Cole, head, department of surgery, Chicago Professional Colleges of the University of Illinois. Dr. Cole, who is also surgeon-in-chief at the University of Illinois Hospitals, also received honorary fellowship in the Royal College of Surgeons of Edinburgh, Scotland.——Dr. John A. D. Cooper, professor of biochemistry and assistant dean of Northwestern University Medical School, left July 11 for South America to give a month-long course at the University of Buenos Aires on the use of radioisotopes in medicine.——The annual achievement award, given by the Immigrants' Protective League to a distinguished citizen of foreign birth, was presented to Dr. John J. Sheinin, president of Chicago Medical School, on April 17th. Dr. Sheinin received this honor for his "important accomplishments in the field of education."—Dr. Ladislas J. Meduna has announced his resignation as president of the Brain Research, Incorporated, effective April 1.

KANSAS

Dedicate Rehabilitation Center.—The Children's Rehabilitation Unit of the University of Kansas Medical Center, Kansas City, a new building consisting of two stories and a basement and providing 28,500 square feet of classrooms, treatment rooms, play areas and offices, was dedicated May 25. It is connected with the rest of the buildings in the medical center by a tunnel entrance into the basement. The unit will be used primarily to train teachers and technicians in the care of handicapped children. University students in medicine, speech therapy, education, psychology, and social work will receive clinical experience at the unit. Assistant dean Dr. Cecil A. Miller is medical director of the unit and Dr. Louise de Schweinitz has been appointed intake officer. The $375,000 project was built without state tax money. The cost of construction and furnishings was provided from private contributions and Hill-Burton funds. An award of $45,000 a year renewable each year for five years has been received from the Children's Bureau of the United States Department of Health, Education, and Welfare.

The Children's Rehabilitation Unit, University of Kansas Medical Center, Kansas City.

KENTUCKY

Memorial Marker for Dr. Northcutt.—Late this summer, or in the early fall, the dedication and unveiling ceremony of the marker in honor and memory of the late Dr. Joseph Doniphan Northcutt will be held in Devou Park, Covington. Permission to erect this marker was granted to a memorial committee composed of a group of physicians and surgeons of Campbell and Kenton counties. Dr. Northcutt was born in 1881 in Bracken County and died in 1956 in Kenton County. He was a fellow of the American College of Surgeons.

MARYLAND

Appoint Director of Department of Pathology.—Dr. Ivan L. Bennett Jr., professor of medicine, Johns Hopkins University School of Medicine, Baltimore, has been appointed professor and director of the department of pathology in the university and pathologist-in-chief to the Johns Hopkins Hospital. Dr. Bennett succeeds as Baxley Professor and director of pathology, Dr. Arnold R. Rich, who is retiring after 43 years' association with the Hopkins medical institutions. Dr. Bennett becomes the fourth person to hold these appointments. He first came to the university as assistant in pathology, 1949-50, then joined the resident medical staff at Duke University Hospital, Durham, N. C., 1950-51, and served 1951-52 as resident in medicine at Grady Hospital, Atlanta, Ga. He returned to Hopkins in 1954 from Yale University, New Haven, Conn., where he was assistant professor of medicine. In 1957, Dr. Bennett was promoted from associate professor to professor.

Personal.—Appointment to the National Advisory Heart Council of Dr. Edwin C. Andrus, associate professor of medicine and chief of the division of cardiology, department of medicine, Johns Hopkins University Medical School, Baltimore, has been announced.——Detlev W. Bronk, LL.D., president of the Rockefeller Institute, has announced the election of Philip Bard, Ph.D., dean of the medical faculty and professor of physiology, Johns Hopkins University School of Medicine, Baltimore, to the institute's board of trustees.——The Surgeon General of the U. S. Public Health Service has anannounced the appointment of Dr. Arnold B Kurlander, of Bethesda, to the newly created post of Assistant Surgeon General for Operations. Dr. Kurlander will assist in coordinating the programs of the service's three major operating bureaus and perform special assignments for the Surgeon General.

MICHIGAN

George Kamperman Annual Lectureship Instituted.—On March 27 Wayne State University College of Medicine, Detroit, officially notified Dr. George A. Kamperman of the institution of the George Kamperman Annual Lectureship of Wayne State University College of Medicine, and personally handed to him a citation. Dr. Kamperman was chief of the department of obstetrics and gynecology at Harper Hospital, Detroit, from 1922-1945. Since his retirement he was appointed a member of the board of trustees of Harper Hospital. He was a founding member and first president of the Detroit Gynecological Society and again served as president when this society was reorganized to form the Michigan Society of Obstetricians and Gynecologists. He was a founding member of the Central Association of Obstetricians and Gynecologists and is a past-president of this organization. He is a fellow of the American College of Surgeons.

MISSOURI

Teachenor Memorial Fund.—A memorial fund has been established to honor the late Dr. Frank Randall Teachenor who helped pioneer the specialty of neurological surgery. Under the organization of a Teachenor Memorial Committee, contributions are being received to build a Frank Randall Teachenor Memorial Operating Theater in the new Research Hospital Medical Center at Kansas City. Anyone wishing to participate may make a contribution to the Frank Randall Teachenor Memorial Fund Committee in care of the Research Hospital, 23rd and Holmes Streets, Kansas City, Mo.

Summer Fellowships for Students.—Twenty-four students at the Saint Louis University School of Medicine have been awarded 1958 summer fellowships totaling $14,800 and are engaged in research projects ranging from 8 to 12 weeks of study. The student research program is supported by awards from the U. S. Public Health Service, Lederle Laboratories, Cancer Research Fund, Tobacco Industry, National Foundation for Infantile Paralysis, Allergy Foundation of America, Children's Research Foundation, and Saint Louis University Biochemistry Committee on Grants. The summer fellowships are awarded annually "to provide an opportunity for the medical students to have first hand experience with research problems" and do not substitute for any of the regular school requirements. Students are selected on the basis of their own initiative and interest, providing they qualify in academic standing. Each project is created by the student and is submitted to the scrutiny of faculty members.

NEW YORK

Annual Postgraduate Week.—The second annual Postgraduate Week of the New York Academy of Medicine will be held Oct. 13-17 with the theme "Research Contributions to Clinical Practice." A total of 15 lectures will be presented under the following panel headings and chairmen:

The Diagnosis and Management of Cerebral Vascular Diseases, Dr. Irving S. Wright, Cornell University Medical College.
Influenza and Upper Respiratory Infections, Dr. Walsh McDermott, Cornell University Medical College.
Glomerulonephritis and Pyelonephritis, Dr. William Goldring, New York University College of Medicine.
Potassium Therapy, Dr. Saul J. Farber, New York University College of Medicine.
The Radiation Hazard, Dr. Joseph E. Rall, National Institutes of Health, Washington, D. C.

A scientific exhibit is planned. Registration is required of nonfellows of the academy, though no fee will be charged. For information write Dr. Robert L. Craig, Secretary, New York Academy of Medicine, 2 E. 103rd St., New York 29.

New York City

Laboratory for Research in Reproduction.—A fertility research laboratory has been established at the Margaret Sanger Research Bureau for the purpose of studying the physiology of reproduction as well as evaluating methods for the control of conception. Studies on sperm migration, the time required for the sperm to enter the cervix, and other reproductive processes are already under way. Over 70 products that are being used for contraceptive purposes have been studied and evaluated in the bureau's research laboratories. The work is under the direction of Dr. Abraham Stone, director of the bureau, and John MacLeod, Ph.D., of Cornell University.

Personal.—Dr. James T. Daniels Jr., associate professor of neurosurgery at New York University–Bellevue Medical Center Post-Graduate Medical School, has accepted the post of director of research of the new Misericordia General Hospital. He will direct the research staff in applied and basic medical research, and will continue in his position of chief of neurosurgery. The new 9-million-dollar general hospital is in its final construction stages.——Dr. Charles A. Ragan Jr., professor of clinical medicine, Columbia University College of Physicians and Surgeons, has been appointed to serve through September, 1962, on the National Advisory Arthritis and Metabolic Diseases Council.

NORTH DAKOTA

State Medical Election.—Dr. Oliver A. Sedlak, Fargo, was elected president of the North Dakota State Medical Association at its annual meeting in Minot. Other officers include: Dr. John C. Fawcett, Devils Lake, president-elect; Dr. Carroll M. Lund, Williston, first vice-president; Dr. Edwin H. Boerth, Bismarck, second vice-president; Dr. G. Alfred Dodds, Fargo, speaker of the House of Delegates; Dr. Ralph E. Leigh, Grand Forks, vice-speaker; Dr. Richard D. Nierling, Jamestown, secretary; Dr. Ernest J. Larson, Jamestown, treasurer; and Dr. Willard A. Wright, Williston, delegate to the American Medical Association.

OHIO

Handbook for Treatment of Radiation Accidents.—At the request of the Atomic Energy Commission, a handbook for physicians who must treat victims of serious radiation or nuclear accidents is being compiled by the University of Cincinnati College of Medicine department of radiology and radioisotope laboratory, in cooperation with the AEC's *division of biology and medicine.* Dr. Eugene L. Saenger, director of the radioisotope laboratory and associate clinical professor of radiology, is editor and chairman of the handbook committee. The AEC has given a $5,600 two-year grant for the work. The handbook will outline possible accidents and will list emergency procedures for exposed humans and the accident area and guide the collection of data to be used in preparation for future accidents. Assisting Dr. Saenger with the manual are Dr. Charles M. Barrett, professor of therapeutic radiology and Dr. Mitchell R. Zavon, assistant professor of industrial medicine, both of Cincinnati university, and Dr. Joseph A. Quigley, of the National Lead Co., at Fernald.

PENNSYLVANIA

Expand Program in Nuclear Technology.—The University of Pittsburgh has been awarded a $30,000 grant by the Atomic Energy Commission for the acquisition of equipment and instruments to be used in the teaching of nuclear technology as applied to the life sciences. The award supports an expanded program of training in radiation health within the university's department of occupational health. The program was recently established by a 10-year grant from the Rockefeller Foundation. Dr. Niel Wald will head the Pittsburgh radiation health program faculty. Dr. Wald served the department of radiobiology, USAF School of Aviation Medicine, for two years. In 1954, he joined the National Research Council's Atomic Bomb Casualty Commission in Hiroshima as senior hematologist for three years. Other members of this training group are Prof. Herman Cember, Dr. Albert A. Spritzer, and Mr. Joseph A. Watson. This group is responsible for the radiation health program on the campuses of the university and of the Carnegie Institute of Technology, as well as in industrial establishments and hospitals in the community. Physicians interested in advanced training in radiation health should address inquiries to the Secretary, Graduate School of Public Health, University of Pittsburgh, Pittsburgh 13.

Personal.—George Denton Beal, Ph.D., will retire as a director of research at Mellon Institute Aug. 31, after 32 years of service. For 25 years Dr. Beal took part in the periodic revision of the United States Pharmacopeia. He is president of the American Council on Pharmaceutical Education, and a member of the Board of Trustees of the convention which prepares the Pharmacopeia.——Dr. Edmund R. McCluskey, professor and head of the department of pediatrics, University of Pittsburgh, has been named vice-chancellor of the schools of the health professions at the university, effective July 1. He succeeds Dr. Robert A. Moore, who resigned to become president of the Downstate Medical Center of the State University of New York.——Dr. Robert J. Halen, Pittsburgh, has been appointed Works Physician at the Pittsburgh Works of Jones & Laughlin Steel Corporation, succeeding Dr. C. Merle Bundy, Pittsburgh, who has resigned.

Philadelphia

University Lecture.—Dr. George Rosen, Columbia University Faculty of Medicine, New York City, will give the first annual Victor Robinson Lecture in History of Medicine at Temple University School of Medicine Sept. 23, 4-5 p. m., in the medical school auditorium. This lectureship is named in honor of Dr. Victor Robinson, professor of history of medicine at Temple University from 1929 until his death in 1947. Dr. Rosen is editor of the *American Journal of Public Health.*

TENNESSEE

Dr. Patterson Appointed Dean at Vanderbilt.—The appointment of Dr. John W. Patterson as director of medical affairs and dean of the Vanderbilt University School of Medicine, Nashville, has been announced. Dr. Patterson, dean of the Faculty of Medicine at the University of British Columbia, Vancouver, Canada, will come to Vanderbilt in September to succeed Dr. John B. Youmans, who is resigning to become head of medical research for the U. S. Army. Dr. Patterson, who lived in India from the age of 3 until he was 18, taught chemistry for a year at the University of Vermont before he and his wife began the study of medicine at Western Reserve, Cleveland, where she became a pediatrician and he a teacher of anatomy and associate dean of the medical school. He has been dean at British Columbia since 1956.

TEXAS

Texas Gerontological and Geriatrics Societies Merge.—Final plans for the merging of the Texas Gerontological Society and the Texas Geriatrics Society have been made. The Texas Geriatrics Society, organized in 1955, has been open to physicians. The Texas Gerontological Society, organized in 1956, has been open to professional and lay members interested in aging. The merged groups will have membership in excess of 500 and will work closely with the special committee created by the Texas Legislature in May, 1957, to study the problems of the aged. The new society will have five divisions: clinical medicine, biological sciences, psychological and social sciences, social work and administration, and general membership. Officers will be elected following the annual meeting of the Texas Gerontological Society, in Austin, Nov. 14-15, at the Driskell Hotel. For information write Mr. Herbert Shore, president, Texas Gerontological Society, 2525 Centerville Road, Dallas 28, Texas.

VERMONT

Internists Form State Chapter.—A Vermont Chapter of the American Society of Internal Medicine is being organized. The initial meeting was held in Middlebury in early June. Dr. William A. Pratt, Rutland, was elected temporary chairman; Dr. Robert A. Walker was appointed chairman of a committee to develop a constitution and by-laws; Dr. Robert E. O'Brien, 11 Mansion St., Winooski, was selected as chairman of the committee to contact charter or founding members. Charter members are those who are diplomates of the American Board of Internal Medicine or members of the American College of Physicians. Others, who limit their practices to internal medicine, may apply for membership following the adoption of the constitution and by-laws.

WASHINGTON

Plan Institute for Heart and Cancer Research.—Preliminary plans for the S. Maimon Samuels Institute for Heart and Cancer Research have been approved by the Board of Regents, University of Washington, Seattle. To be built attached to the south wing of the University's Teaching and Research Hospital, the three-story building will be devoted entirely to heart and cancer research laboratories, with the exception of an entrance and waiting room. A major portion of the cost, estimated at $800,000, was a gift of Dr. and Mrs. S. Maimon Samuels, of Seattle. Construction is scheduled to start within a year.

WEST VIRGINIA

Annual Meeting in White Sulphur Springs.—The 91st annual meeting of the West Virginia State Medical Association will be held Aug. 21-23 at The Greenbrier, White Sulphur Springs. Dr. Charles A. Hoffman, of Huntington, president of the association, will present an address at the opening session. The program includes the following papers by out-of-state speakers:

Allergic Reactions of the Respiratory System, Including Sinus Involvement, Dr. J. Warrick Thomas, Richmond, Va.
Practical Considerations in the Use of Blood, Dr. Paul I. Hoxworth, Cincinnati.
Obesity, Vitamins and Women, Dr. Philip Thorek, Chicago.
Urological Emergencies, Dr. Theodore R. Fetter, Philadelphia.
Gas, Smother and Choke, Dr. David M. Little Jr., Hartford, Conn.
Surgical Emergencies, Dr. Vinton E. Siler, Cincinnati.
Endarterectomy for Coronary Artery Disease, Dr. Charles P. Bailey, Philadelphia.
Stress as a Therapeutic Friend, Dr. Howard A. Rusk, New York City.

A special discussion, "Investment Program for the Physician," will be held the morning of Aug. 23. Technical and scientific exhibits and motion-picture sessions are planned. Entertainment includes golf and skeet and trap shooting tournaments. For information write the West Virginia State Medical Association, Box 1031, Charleston 24, W. Va.

Personal.—Dr. Joseph M. Parker, superintendent of Hawthornden State Hospital near Cleveland, Ohio, has accepted an appointment as superintendent of Barboursville State Hospital, succeeding Dr. William S. Sadler.——The College of William and Mary June 8 bestowed upon Dr. Walter E. Vest, of Huntington, the honorary degree of master of arts "in appreciation of scholarship and service to humanity." Benjamin Franklin was the first to receive this honorary degree (in 1756). A few such degrees were conferred in the mid-decades of the nineteenth century; however, Dr. Vest is the first to be given the degree honoris causa in the twentieth century.——Dr. Richard J. Lilly, of Topeka, Kansas, formerly of Pontiac, Mich., has been appointed superintendent of Weston State Hospital (mental), at Weston. He succeeds Dr. Azby A. Milburn, who has been acting superintendent at the institution since Dr. H. Sinclair Tait resigned in April, 1957, to accept appointment as senior psychiatrist at the VA Regional Office in Wheeling.

GENERAL

Symposium on Pulmonary Diseases in Denver.—The 11th annual Pulmonary Diseases Symposium will be conducted at Fitzsimons Army Hospital, Denver, Sept. 8-12. Students representing the Armed Services, Veterans Administration, U. S. Public Health Service, state and local institutions, as well as private practitioners, are invited. Fitzsimons Army Hospital is the Army's center for chest and pulmonary diseases. Instructors for this symposium will be chosen from its specialists and from the staff of the University of Colorado Medical School. For information write the Public Information Office, Fitzsimons Army Hospital, Denver 8.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 19, 1958		July 20, 1957 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	1
New Hampshire	..	..	..
Vermont	..	1	..
Massachusetts	..	..	2
Rhode Island	..	..	..
Connecticut	..	..	3
Middle Atlantic States			
New York	3	6	7
New Jersey	2	3	..
Pennsylvania	..	..	3
East North Central States			
Ohio	1	6	10
Indiana	1	1	4
Illinois	1	4	13
Michigan	1	4	10
Wisconsin	1	3	15
West North Central States			
Minnesota	..	2	2
Iowa	..	..	2
Missouri	1	2	6
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	1	4
Kansas	..	5	4
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	1	3	..
Virginia	3	5	2
West Virginia	..	1	2
North Carolina	1	2	17
South Carolina	..	..	6
Georgia	..	..	2
Florida	8	23	2
East South Central States			
Kentucky	1	1	8
Tennessee	1	5	7
Alabama	..	..	2
Mississippi	..	6	8
West South Central States			
Arkansas	1	2	4
Louisiana	1	1	9
Oklahoma	1	2	11
Texas	15	24	33
Mountain States			
Montana	2	3	1
Idaho	..	1	1
Wyoming	..	..	..
Colorado	1	1	..
New Mexico	..	..	4
Arizona	..	..	2
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	5
California	5	7	37
Territories and Possessions			
Alaska	..	..	..
Hawaii	7	7	..
Puerto Rico	3	3	2
Total	62	135	254

Personal.—Dr. Carlos Luis Gonzalez, of Venezuela, formerly minister of health and social welfare, assumed the duties of assistant director of the Pan American Sanitary Bureau in Washington, D. C., June 16. He studied at the School of Hygiene of Johns Hopkins University of Baltimore, first with a grant from the Rockefeller Foundation and then with one from his government, obtaining the degree of doctor of public health in 1948. He was a member of the executive board of the World Health Organization and also delegate from Venezuela to the first Inter-American Congress of Hygiene which met in Havana in 1952.

Statement on BCG by Chest Physicians.—The Executive Council of the American College of Chest Physicians at an annual meeting recently held in San Francisco passed the following resolution: "In view of the vital interest in improving public health and welfare, and in the eradication of diseases of the chest in particular, our position regarding the use of BCG (bacillus Calmette-Guerin) against tuberculosis in the United States should be made known. At the present time, there is insufficient evidence that significant protection is afforded by its use. The Council fully endorses the antituberculosis control program of the U. S. Public Health Service, which includes research in BCG, and urges the continued support of their program."

Medical Research Fellowships and Grants.—The Life Insurance Medical Research Fund is receiving applications for two types of awards to be available July 1, 1959, as follows: (1) Until Oct. 15, for postdoctoral research fellowships. Candidates may apply for support in any field of the medical sciences. Preference is given to those who wish to work on fundamental problems, especially those related to cardiovascular function or disease. Minimum stipend is $3,800, with allowances for dependents and necessary travel. (2) Until Nov. 1, for grants to institutions in aid of research on cardiovascular problems. Support is available for physiological, biochemical, and other basic work related to cardiovascular problems as well as for clinical research in this field. Information and application forms may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 345 E. 46th St., New York 17.

National Allergy Month.—Sponsored by the Allergy Foundation of America, the second annual National Allergy Month has been announced for Aug. 15-Sept. 15. A free pamphlet, "Hay Fever and Other Allergic Diseases," has been prepared by the foundation as part of the program of public information and education and may be obtained by writing to P. O. Box 1005, Grand Central Station, New York City 17. The foundation furnishes information, gives guidance to those seeking medical care, supports research and training programs, and "seeks to improve facilities for clinical and hospital care." It works closely with the American Academy of Allergy, the American College of Allergists, and the National Institute of Allergy and Infectious Diseases of the U. S. Public Health Service. Dr. Charles D. Marple, New York City, is the director of the foundation. For information write the Allergy Foundation of America, 801 Second Ave., New York 17.

Foundation for Research in Neurological Diseases.—The National Neurological Research Foundation has been organized and chartered in Washington, D. C., "to provide research into the prevention and cure of chronic, progressive disorders of the nervous system" by establishing fellowships and by supporting research for work in the neurological field. The distribution of fellowships and research projects, as funds become available, will be directed by a Scientific Advisory Committee, comprised of the following: Dr. Raymond D. Adams, Boston; Edward W. Dempsey, Ph.D., Dr. Oliver H. Lowry and Dr. James L. O'Leary, St. Louis; Dr. Louis S. Goodman, Salt Lake City; Dr. Seymour S. Kety, Bethesda, Md.; Horace W. Magoun, Ph.D., Los Angeles; and Dr. A. Earl Walker, Baltimore. The fellowships will be $10,000-$12,000 a year, for a period of five years. The foundation will supplement the activities of existing organizations. Money will be raised by contributions from the public and from foundations. For information write the National Neurological Research Foundation, 3255 N Street, N. W., Washington 7, D. C.

Western Surgeons Meeting in Reno.—The Western Regional Meeting of the United States Section of the International College of Surgeons will be held Aug. 21-23 at the Riverside Hotel, Reno, Nevada. An opening day panel on problems in general practice will be moderated by Dr. Ross T. McIntire, Chicago, executive director of the college. About 25 papers will be presented. Speakers will include: Drs. Franz K. Bauer, James N. Wilson, and Telfer B. Reynolds, Los Angeles; Gerald B. O'Connor, George W. Pierce, and Charles P. Mathe, San Francisco; Edward L. Compere, Chicago; A. James McAllister, Salt Lake City; Roger Anderson, Seattle; Robert P. O'Donnell, Las Vegas; Harry E. Bacon, Philadelphia, and Col. Clinton S. Maupin, M. C., U. S. Army, Washington, D. C. Dr. Curtice Rosser, Dallas, president of the U. S. Section, will present "Polyps of the Large Bowel" the afternoon of Aug. 21. Medical motion picture sessions, exhibits, question-and-answer periods, and a ladies' program are arranged. The American Academy of General Practice will give its attending members category II credit. Membership in the college is not required for attendance. For information write Dr. Frederick M. Anderson, 275 Hill St., Reno, Nev., general chairman.

CANADA

International Meeting on Genetics in Montreal.—The 10th International Congress of Genetics will be held Aug. 20-27 at McGill University, Montreal. The presidential address will be given Aug. 20 by Sewall Wright, LL.D. The program has over 40 topics, including multiple sessions of the following: "Mutations Induced by Ionizing Radiations," "Plant Cytology," "Biochemical Genetics," "Human and Medical Genetics," and "Animal Breeding." The Huskins Memorial Lecture will be held Aug. 19, 8 p. m., in the auditorium of the University of Montreal. Exhibits and pre- and post-congress tours are planned. Registration fee is $7.50 (Canadian). For information write the X International Congress of Genetics, McGill University, Montreal 2, Province of Quebec, Canada.

LATIN AMERICA

Congress on Mental Health in Peru.—The third Latin American congress on Mental Health will be held Oct. 27-Nov. 1 in Lima, Peru. The program will be presented under the following six general topics:

Mental Illness in Urban and Rural Areas.
Problems of Mental Health Dependents of Internal and External Migration.
Chronic Intoxication in Latin America.
Work and Mental Health.
Organization of the Community.
Social Problems of the Community.

Twenty-two sub-topics are arranged under the major themes. Physicians from the United States and Canada are invited to present papers. For information write Dr. Prado Baltazar Caravedo, Secretario General, III Congreso Latino-Americano de Salud Mental, Departamento de Higiene Mental, Natalio Sánchez 215, 3er. Piso, "G", Lima, Perú.

FOREIGN

International Meeting on Neuro-Psychopharmacology in Rome.—Organized by the Collegium Internationale Neuro-Psychopharmacologicum, the first international meeting on neuropsychopharmacology will be held in Rome Sept. 8-12 under the presidency of Prof. Ernest Rothlin, Basle, Switzerland, and Prof. Emilio Trabucci, (president of the Rome meeting). Titles for the two plenary sessions are: "The Present Status of Neurochemistry" and "The Impact of Psychotropic Drugs on the Structure, Function and Future of Psychiatric Services (a) in the hospitals and (b) in extra-mural clinics and private practice." The following symposiums are planned:

Methods and Analysis of Drug-Induced Abnormal Behavior in Animals.
Methods and Analysis of Drug-Induced Abnormal Mental States in Man.

Comparison of Abnormal Behavioral States Induced by Psychotropic Drugs in Animals and Man.
Comparison of Drug-Induced and Endogenous Psychoses in Man.

The official languages will be English, French, Italian, and German, with simultaneous translations available for the first three languages. At a reception at Campidoglio, Professor Rothlin, will present an address, and at a reception at Castel Gandolfo, the group will be addressed by His Holiness, Pope Pius XII. For information write Dr. Herman C. B. Denber, Manhattan State Hospital, 600 E. 125th St., New York 35.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

American Board of Dermatology: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 20, 1958. *Oral.* Chicago, Oct. 13-16. *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application is Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application is Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), January 1959. Final date for filing application was July 1, 1958. *Oral Examinations 1958* (Part II): Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Chicago, Oct. 24-26 and New York, *Dec.* 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Chicago, Oct. 9-11. *Final* date for receipt of case reports was July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Preventive Medicine: *Examination in Public Health.* St. Louis, Oct. 24-26. Final date for filing application was Aug. 15. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination.* Washington, D. C., Dec. 8-11. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application is Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Philadelphia, Sept. 15-16; Rochester, Minn., Oct. 20-21; Nashville, Tenn., Nov. 17-18; New York City, Dec. 15-16; Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: Various centers throughout the United States. *Written.* Spring of 1959. Final date for filing application is December 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Avenue, Detroit 2.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

NAVY

Aviation Medicine Training Program.—The new graduate training program of the Naval School of Aviation Medicine at Pensacola, Fla., is designed to prepare selected flight surgeons for certification in aviation medicine by the American Board of Preventive Medicine. The program was reviewed in May, 1955, when the American Board of Preventive Medicine convened at the School of Aviation Medicine with representatives of the American Medical Association. Department heads and faculty were interviewed at length to determine their qualifications, teaching methods, and experience, and the school was approved for two years' formal credit in Aviation Medicine by the American Board of Preventive Medicine in the summer of 1956.

Lieut. Commander David P. Morris, M. C., U. S. N., on July 16, 1958, became the first naval medical officer to complete residency training in aviation medicine at the school. Dr. Morris served as flight surgeon at NAS, Columbus, Ohio, and at Sangley Point in the Philippines. In preparation for residency training in aviation medicine, he spent a year at the Johns Hopkins University School of Hygiene and Public Health. He has published and collaborated in the authorship of several research papers, including "Reduction of Metabolic Rate at Simulated High Altitude" and "Studies on Oxygen Toxicity During Heavy Work." He now assumes his new billet as senior medical officer and flight surgeon aboard the USS Essex.

The newly commissioned U. S. Naval Dispensary at Rota, Spain.

One Hundred Ninety-two Receive Internship Certificates.—The surgeon general has announced that as of July 3, 1958, 192 Navy Medical Corps lieutenants had completed their internship training under the Navy's one-year rotating internship training program. They received their internship certificates at 14 of the Navy's 23 continental United States hospitals where internship training is administered. A number of the graduated officers are being assigned to duty at medical department activities at sea and ashore, while others will receive further training in their particular specialties.

VETERANS ADMINISTRATION

Personal.—Dr. George E. Armstrong, New York City, director of the New York University–Bellevue Medical Center and formerly surgeon general of the Army, has been made chairman of the VA Special Medical Advisory Group, succeeding Dr. Robert M. Zollinger of Columbus, Ohio, whose term as chairman expired June 30. The group meets quarterly to advise the Administrator of Veterans Affairs on matters related to medical care and treatment of veterans.

PUBLIC HEALTH SERVICE

Report on Disability.—Due to illness or injury, the American people stayed home from work, stayed in bed, or otherwise cut down on normal activities for a total of 662,800,000 days during the period July-September, 1957. If this rate were applied to a full year, the number of days of restricted activity would average about 16 per person per year. These estimates are contained in a report by the Public Health Service "Preliminary Report on Disability, United States, July-September 1957." The report includes all age groups. As of August, 1957, about 17 million persons, or 10% of the population, had chronic health conditions which caused continuing limitations in their normal activities. Women and girls accounted for more days of restricted activity than men and boys, averaging 17.5 days per year as compared with 14.1 for males. Children under 5 years of age averaged 6.4 days a year of restricted activity, while people 65 years and over averaged 44.4. An estimated 227.9 million patient-days were spent in bed, a rate of about 5.5 days in bed for each person a year. The number of man-days lost from work was about 126,800,000 during the quarter, which amounts to an annual rate of 7.9 work-loss days for each employed person during the year. Copies of the new report may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., for 30 cents each.

Dr. Hoge Accepts Post in Chicago.—Dr. Vane M. Hoge, who is retiring from the Public Health Service after 30 years of service, has been appointed executive director of the newly-created Hospital Planning Council of Metropolitan Chicago, effective Sept. 15. The council was organized early this year by a group of Chicago business and civic leaders to aid in planning new and improved hospital facilities necessary for the rapidly growing metropolitan area. Dr. Jack C. Haldeman has been appointed chief of the Division of Hospital and Medical Facilities of the Public Health Service to succeed Dr. Hoge.

DEATHS

Abell, Nathan Douglas, Louisville, Ky.; University of Louisville Medical Department, 1909; also a graduate in pharmacy; member of the Kentucky State Medical Association; died June 18, aged 83, of chronic pyelonephrosis and arteriosclerotic heart disease.

Albrecht, Henry Francis, Sand Lake, N. Y.; Albany (N. Y.) Medical College, 1906; an associate member of the American Medical Association; for many years health officer of Green Island, N. Y.; physician for Selective Service during World War II; on the honorary staff, St. Mary's Hospital in Troy; died June 8, aged 74, of acute myocardial infarction.

Argabrite, Otho Paul, Alderson, W. Va.; University of Maryland School of Medicine, Baltimore, 1907; died June 12, aged 74, of heart disease.

Atlas, Lawrence N. Ⓜ Laguna Beach, Calif.; born in Akron, Ohio, Aug. 8, 1906; Western Reserve University School of Medicine, Cleveland, 1930; served on the faculty of his alma mater and the University of Southern California School of Medicine in Los Angeles; fellow of the American College of Surgeons; member of the Central Society for Clinical Research; practiced in Los Angeles, where he was on the staffs of the Hospital of the Good Samaritan, Mount Sinai, Los Angeles County, and Cedar of Lebanon hospitals, and the St. Joseph Hospital in Burbank; died in the Hoag Memorial Hospital in Newport Beach May 20, aged 51.

Bartling, Carl Herman Ⓜ Rockford, Ill.; Northwestern University Medical School, Chicago, 1913; member of the American Society of Anesthesiologists; specialist certified by the American Board of Anesthesiology; interned at the Cook County Hospital in Chicago; veteran of World Wars I and II; served on the staff of the Veterans Administration Hospital Center in Temple, Texas; retired from the Veterans Administration May 31, 1955; on the staffs of Rockford Memorial and St. Anthony hospitals; died in the Veterans Administration Hospital in Hines June 8, aged 68, of bilateral bronchopneumonia.

Beam, Albert Ⓜ Americus, Kan.; University Medical College of Kansas City, Mo., 1908; on the staff of the Newman Memorial County Hospital, Emporia, June 1, aged 86.

Black, Walter Munro, St. Marys, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1898; formerly associated with the Eastern State Penitentiary; died June 12, aged 84.

Bohrer, Edward Royse Ⓜ Jefferson City, Mo.; Washington University School of Medicine, St. Louis, 1934; secretary of the Missouri State Medical Association; member of the American Academy of General Practice; secretary of the Cole County Medical Society; veteran of World War II; on the staff of the state division of health; on the staff of St. Mary's Hospital; died June 4, aged 49, of arteriosclerotic heart disease.

Bowman, William Townzen, Greenview, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1906; died in St. John's Hospital in Springfield June 9, aged 84.

Boyer, Samuel P., Brooksville, Fla.; University of Pittsburgh School of Medicine, 1916; veteran of World War I; died in the Hernando County Hospital June 10, aged 76, of lymphosarcoma.

Busbee, Olin Dantzler, Springfield, S. C.; Medical College of the State of South Carolina, Charleston, 1911; served as mayor; veteran of World War I; died in the Veterans Administration Hospital, Columbia, June 9, aged 70, of hypertension, arteriosclerotic heart disease with myocardial infarction and diabetes mellitus.

Chideckel, Maurice, Baltimore; College of Physicians and Surgeons, Baltimore, 1908; also a rabbi; author of many books; died June 20, aged 75, of coronary arteriosclerosis.

Clement, John B. Ⓜ Lester Prairie, Minn. (licensed in Minnesota in 1900); died in Glencoe May 10, aged 82, of heart disease.

Cole, William Andrew Ⓜ Savannah, Ga.; University of Georgia Medical Department, Augusta, 1913; specialist certified by the American Board of Radiology; on the staff of the Warren Candler Hospital, where he died June 13, aged 74, of cardiac decompensation.

Colgan, Robert Clinton Ⓜ Bridgeport, Pa.; University of Pennsylvania School of Medicine, Philadelphia, 1925; specialist certified by the American Board of Otolaryngology; veteran of World War I; on the faculty of the University of Pennsylvania Graduate School of Medicine in Philadelphia, where he was on the staff of the Hospital of the University of Pennsylvania; died June 7, aged 59, of myocarditis with coronary sclerosis.

Cummer, Clyde Lottridge Ⓜ Cleveland; born in Cadillac, Mich., Feb. 23, 1882; Western Reserve University Medical Department, Cleveland, 1907; from 1909 to 1946 on the faculty of his alma mater,

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Ⓜ Indicates Member of the American Medical Association.

where he served successively as teacher and associate professor of clinical pathology and assistant clinical professor of dermatology and syphilology; specialist certified by the American Board of Dermatology and Syphilology; at one time chairman of the public health council of the Ohio Department of Health; formerly member of the Council on Scientific Assembly, member of the House of Delegates, and chairman of the Section on Dermatology and Syphilology of the American Medical Association; past-president of the Ohio State Medical Association; for many years treasurer of the American Academy of Dermatology and Syphilology, of which he was past-president; past-president of the Academy of Medicine of Cleveland and was the winner of its 1942 distinguished service award; past-president of the Cleveland Medical Library Association, serving as chairman of the board from 1929 to 1937 and secretary of the committee for building the Allen Memorial Library Building from 1923 to 1926; member of the American Dermatological Association; past-president of the Cleveland Dermatological Society; honorary consultant for the U. S. Army Medical Library from 1942 to 1946; during World Wars I and II was on advisory medical boards for selective service; in the Korean War was a member of the board of medical appeals for the northern district of Ohio; member of Phi Beta Kappa, Beta Theta Pi, Nu Sigma Nu, Alpha Omega Alpha, and Sigma Xi fraternities; at various times on the staffs of St. Alexis, City, St. John's, and St. Vincent Charity hospitals; contributor to "Blakiston's New Gould Medical Dictionary" in 1949; author of "A Manual of Clinical Laboratory Methods"; died in the Hanna House, University Hospital June 7, aged 76, of adenocarcinoma of the kidney.

Davis, Walter William Ⓢ Los Angeles; Meharry Medical College, Nashville, Tenn., 1935; certified by the National Board of Medical Examiners; served on the staffs of Methodist Hospital of Southern California, Queen of Angels Hospital, and Temple Hospital; died June 8, aged 48, of acute myocardial infarction.

Dietzel, Marie P. Delalondre, Galveston, Texas; University of Texas School of Medicine, Galveston, 1897; died in the John Sealy Hospital June 6, aged 79, of mesenteric thrombosis and atherosclerosis.

Draper, Willard Jesse Ⓢ Heber, Utah; Northwestern University Medical School, Chicago, 1948; member of the American Academy of General Practice; on the county school board; city health officer; co-owner of Heber Hospital; died June 4, aged 37, of an accidental gunshot wound.

Driscoll, Jerome James, Danbury, Conn.; University of Vermont College of Medicine, Burlington, 1925; died in the Danbury Hospital May 31, aged 57, of subdural hemorrhage due to a skull fracture as the result of a fall.

Eggers, Maynard Woodrow Ⓢ Sioux Falls, S. D.; Northwestern University Medical School, Chicago, 1939; formerly clinical assistant professor of otorhino-laryngology, University of South Dakota School of Medical Sciences, Vermillion; died June 9, aged 45, of a stab wound, self-inflicted.

Egloff, William Chauncey Ⓢ Mason City, Iowa; Rush Medical College, Chicago, 1927; served as junior associate in medicine at Harvard Medical School in Boston, where he was research fellow in medicine at Peter Bent Brigham Hospital; veteran of World War II; died near Park Rapids, Minn., May 19, aged 57.

Flagg, Mary B. Fimpel, Vancouver, Wash.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; died June 12, aged 77, of arteriosclerosis.

Fletcher, Norton De Los Lull, White Plains, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1902; served as consulting ophthalmologist at Manhattan Eye, Ear and Throat Hospital; died June 20, aged 81.

Fowler, Arthur, Humphrey, Ark.; University of Arkansas School of Medicine, Little Rock, 1907; member of the Arkansas Medical Society; for many years member and president of the school board; in 1952 the gymnasium at the Humphrey High School was named Fowler Hall in his honor; served as mayor; died in Pine Bluff June 9, aged 77, of metastatic melanoma of the left lung and right chest wall.

Frankel, Jerome Stanley Ⓢ Cleveland; Ohio State University College of Medicine, Columbus, 1941; also a Ph.D.; specialist certified by the American Board of Internal Medicine; member of the American Association for the Advancement of Science, American College of Cardiology, and the American College of Allergists; fellow of the American College of Physicians; veteran of World War II; demonstrator of medicine, Western Reserve University School of Medicine; on the staff of the Mount Sinai Hospital, where he died June 1, aged 45, of lymphosarcoma.

Freidman, Louis Lawrence Ⓢ St. Paul; University of Minnesota Medical School, Minneapolis, 1933; clinical assistant professor of obstetrics and gynecology at his alma mater, where he founded and directed the fertility clinic; specialist certified by the American Board of Obstetrics and Gynecology; founding fellow of the American Academy of Obstetrics and Gynecology; fellow of the American Society for the Study of Sterility; a member of the New York Academy of Sciences; served on the medical staffs of Midway and Miller hospitals in St. Paul and Mount Sinai Hospital in Minneapolis; died June 14, aged 50.

Gardner, Cyrus Bunting Ⓜ Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1904; fellow of the American College of Surgeons; past-president of the state board of registration in medicine; on the staffs of the Edward W. Sparrow Hospital and St. Lawrence Hospital, where he died in June, aged 78, of myocardial infarction.

Gatz, Robert Eugene, Fern Creek, Ky.; Hospital College of Medicine, Louisville, 1906; also a graduate in pharmacy; died June 6, aged 73, of cancer.

Gibbs, James C., Sanford, Fla.; Chicago Homeopathic Medical College, 1886; died June 9, aged 102, of cerebral hemorrhage.

Gordon, Aileen Mary Ⓜ Denver; University of Colorado School of Medicine, Denver, 1951; interned at University of Colorado Medical Center; served a residency at the Veterans Administration Hospital; on the staffs of the Mercy and St. Joseph's hospitals, and St. Luke's Hospital, where she died April 25, aged 47, of subarachnoid hemorrhage.

Gowans, Charles W., St. Louis; Washington University School of Medicine, St. Louis, 1899; died June 17, aged 82.

Graham, Henry Flack, Brooklyn; born in Troy, N. Y., April 20, 1880; Columbia University College of Physicians and Surgeons, New York City, 1905; an associate member of the American Medical Association; member of the founders group of the American Board of Surgery; member of the American Surgical Association; fellow of the American College of Surgeons; past-president of the Brooklyn Surgical Society; member of the board of managers of Methodist Hospital, where he was senior consultant; associated with the Mary Immaculate Hospital in Jamaica, Bay Ridge, Victory Memorial, and Norwegian Lutheran hospitals; died June 21, aged 78, of coronary thrombosis.

Haluszczynska, Wera, Providence, R. I.; Friedrich–Alexanders–Universität Medizinische Fakultät, Erlangen, Bavaria, Germany, 1952; interned at the Jersey City Hospital in Jersey City, N. J., where he served a residency; served a residency at the Lynn (Mass.) Hospital and the Rhode Island Hospital; killed in an automobile accident June 21, aged 37.

Harmon, Vachelle Ernest Ⓜ South Bend, Ind.; born in Lebanon, Ky., Sept. 13, 1885; University of Louisville (Ky.) School of Medicine, 1914; member of the Aero Medical Association; formerly member of the board of education, of which he was secretary-treasurer for four years; veteran of World War I; served in the regular Navy; local medical examiner for the Civil Aeronautics Administration; for many years fire and police surgeon; United Air Lines Examiner; on the staffs of the Northern Indiana Children's Hospital, St. Joseph's Hospital, and Memorial Hospital in South Bend, and St. Joseph's Hospital in Mishawaka; died at his summer home in Diamond Lake, Cassapolis, Mich., June 8, aged 72, of coronary occlusion.

Harris, Stevens Thomas, Albuquerque, N. M.; Southern Medical College, Atlanta, 1894; died May 1, aged 85, of arteriosclerosis.

Higgins, Roy Francis Ⓜ Weston, W. Va.; Georgetown University School of Medicine, Washington, D. C., 1918; served on the faculty of his alma mater; fellow of the American College of Surgeons; member of the Medical Society of the District of Columbia; formerly practiced in Washington, D. C., where he was on the staff of the Providence Hospital; on the staff of the Weston State Hospital; died June 20, aged 65, of coronary thrombosis.

Johnson, Frank Dale Ⓜ Waynetown, Ind.; Northwestern University Medical School, Chicago, 1937; past-president of the Montgomery County Medical Society; a staff member of Culver Hospital in Crawfordsville; died June 2, aged 48, of acute coronary heart disease.

Johnson, Walter Lee, San Gabriel, Calif.; Missouri Medical College, St. Louis, 1897; for many years a staff member of Huntington Memorial Hospital in Pasadena, where he died June 9, aged 88, of ruptured arteriosclerotic aneurysm of abdominal aorta.

Kelly, Martin John, Chicago; Loyola University School of Medicine, Chicago, 1917; died June 18, aged 73, of heart disease.

Keogh, Chester Henry, Chicago; Rush Medical College, Chicago, 1899; died June 18, aged 90, of arteriosclerotic heart disease.

Ketron, Lloyd Warren Ⓜ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1911; associate professor emeritus of dermatology at his alma mater, where members of the department of dermatology and the Johns Hopkins Hospital established an annual lecture in his name, the first of which was given this year; specialist certified by the American Board of Dermatology and Syphilology; member of the American Dermatological Association, Society for Investigative Dermatology, and the American Academy of Dermatology and Syphilology; on the staff of the Johns Hopkins Hospital, where he died June 7, aged 73, of arteriosclerotic heart disease, refractory anemia, and pulmonary edema.

Knouf, Clare Elden Ⓜ Iowa City, Iowa; State University of Iowa College of Medicine, Iowa City, 1944; veteran of World War II; member of the American Academy of General Practice and the Iowa Heart Association; resident, department of medicine, Veterans Administration Hospital; hanged himself June 3, aged 39.

Koons, Ruth Alice Ⓜ Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1930; clinical assistant professor of medicine at his alma mater; fellow of the American College of Physicians; on the staffs of the White Cross and Children's hospitals; died in the University Hospital June 9, aged 52.

Leonard, Melville William Ezra, New York City; University of Toronto Faculty of Medicine, Toronto, Ontario, Canada, 1952; interned at Toronto Western Hospital in Toronto, Ontario, Canada; served a residency at the City Hospital in Cleveland and the Metropolitan Hospital in New York City; certified by the National Board of Medical Examiners; on the faculty of the New York Medical College, Flower and Fifth Avenue Hospitals; on the staff of the Metropolitan Hospital; died June 15, aged 34, of coronary disease.

Lewis, Benjamin William Ⓜ Major, U. S. Army, retired, St. Louis; St. Louis University School of Medicine, 1917; received his degree of doctor of public health from Yale University in New Haven, Conn., in 1938; service member of the American Medical Association; entered the medical corps of the U. S. Army in 1918 and retired Dec. 31, 1935, for disability in line of duty; began work with the St. Louis Health Department in 1944 and retired in November, 1956, as chief and physician in the industrial hygiene section; died May 16, aged 65, of coronary occlusion.

Lumsden, Arthur Gomez Ⓜ Petaluma, Calif.; College of Physicians and Surgeons of San Francisco, 1906; served as health officer and secretary of the board of health; on the staff of the Petaluma General Hospital, where he died May 1, aged 75, of coronary disease.

Lyman, Timothy, Sacramento, Calif.; Stanford University School of Medicine, San Francisco, 1915; an associate member of the American Medical Association; veteran of World War I; served on the staff of the Sacramento Hospital; died June 6, aged 75, of heart disease.

Manske, Gerhard Rudolph Ⓜ Texas City, Texas; University of Texas School of Medicine, Galveston, 1932; fellow of the American College of Surgeons; veteran of World War II; associated with the Galveston County Memorial Hospital in La Marque, St. Mary's Infirmary in Galveston, and the Danforth Memorial Hospital; partner of the Beeler–Manske Clinic; charter member and past-president of the Beeler–Manske Clinic; died June 4, aged 52, of coronary occlusion.

Mares, Charles Francis Jr. Ⓜ Galveston, Texas; University of Tennessee College of Medicine, Memphis, 1928; fellow of the American College of Surgeons; served on the faculty of the University of Texas School of Medicine; county physician; on the staff of St. Mary's Infirmary, where he died June 2, aged 58, of acute myocardial infarction.

Mayfield, Carey Boyd, Sesser, Ill.; National University of Arts and Sciences Medical Department, St. Louis, 1912; died April 28, aged 72, of aspiration pneumonia and duodenal ulcer.

Newton, Ralph George Ⓜ Macon, Ga.; Emory University School of Medicine, Atlanta, 1924; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; past-president of the Bibb County Medical Society; served as president of the staffs of Macon and Parkview hospitals; died June 5, aged 60, of coronary occlusion.

Newton, William Curtis, San Diego, Calif.; Boston University School of Medicine, 1896; an associate member of the American Medical Association; veteran of World War I; formerly practiced in Revere, Mass.; died June 6, aged 84, of arteriosclerotic heart disease.

Platt, Paul Campbell Ⓜ Kansas City, Mo.; University of Nebraska College of Medicine, Omaha, 1932; veteran of World War II; on the staffs of the Research and St. Joseph's hospitals; died June 6, aged 53, of coronary occlusion.

Von Der Lieth, Harold Otto, San Francisco; Cooper Medical College, San Francisco, 1897; an associate member of the American Medical Association; served on the staff of Franklin Hospital; veteran of World War I; died in Berkeley, June 7, aged 82, of myocarditis and arteriosclerosis.

Washam, William Worth, Cornelius, N. C.; North Carolina Medical College, Davidson, 1901; on the staff of the Lowrance Hospital in Mooresville, where he died June 2, aged 87, of cardiac fibrillation.

Whitmer, Charles F., Colton, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1898; formerly practiced in East St. Louis, Ill.; a member of the school board when the Colton Union High School district was originally formed and was honored at the dedication of the Charles F. Whitmer Auditorium which stands on the high school grounds; past-president of the Colton Rotary Club; died in the Southern Pacific Hospital, San Francisco, Jan. 1, aged 87, of bronchopneumonia.

Williams, Rodman H., Chaplin, Ky.; University of Louisville (Ky.) Medical Department, 1903; veteran of World War I; died June 8, aged 80, of coronary thrombosis.

Wyatt, James Odis Ⓜ Amarillo, Texas; Meharry Medical College, Nashville, Tenn., 1931; medical superintendent and owner of the M. L. Wyatt Memorial Hospital; died June 3, aged 51, of myocardial infarction and hypertension.

FOREIGN LETTERS

AUSTRIA

Operation for Aortic Stenosis.—At the meeting of the Society of Physicians in Vienna on June 13 Dr. W. Lorbeck reported a series of 20 patients operated on for stenosis of the aortic isthmus. Of these four died postoperatively and in one it was found that the condition was not surgically correctable. The remaining 15 were relieved of their symptoms. The most favorable time for operation was between the 10th and the 20th year of life. Advancing loss of elasticity in the aortic wall leads to disruption of the wound. Dr. F. Kaindl said that selective catheter aortography in combination with the determination of the blood pressure within and above the stenosis was the diagnostic method of choice.

UNITED KINGDOM

Serum Transaminase in Hepatic Disease.—Pryse-Davies and Wilkinson (*Lancet* 1:1249, 1958) carried out more than 1,000 determinations of serum glutamic oxalacetic transaminase (S. G. O. T.) and glutamic pyruvic transaminase (S. G. P. T.) in patients with hepatic and gastrointestinal diseases and in controls. An improved spectrophotometric method was devised, in which the transaminase system was coupled with a second enzymic reaction involving the oxidation of the reduced form of diphosphopyridine nucleotide. It was found that the two transaminases were different entities with different electrophoretic mobilities. They could be separated by paper electrophoresis and acted on different aminoacids. From a study of the serum S. G. O. T. and S. G. P. T. of 157 control subjects it was concluded that values exceeding 40 and 30 units per milliliter respectively are abnormal. The serum S. G. O. T. and S. G. P. T. in patients with a wide range of hepatic diseases were examined. High levels of S. G. O. T. activity (sometimes 2,000 units per milliliter) were observed in patients with acute infectious hepatitis, the highest figures being obtained at the onset of jaundice. The S. G. P. T. was also raised, although not so much. Moderately raised values (100 to 300 units per milliliter) of both enzymes were found in patients with obstructive jaundice, hepatitis due to glandular fever, and toxic hepatitis due to hepatic poisons. Variable results were obtained in patients with cirrhosis and liver metastases; in 64% the S. G. O. T. was raised above normal values, whereas only about 40% showed increased S. G. P. T. activity.

In 35 patients with miscellaneous disease of the gastrointestinal tract not involving the liver, normal values were recorded. The S. G. O. T. showed a moderate and transient rise, up to 300 units per milliliter in patients with myocardial infarction, but in this condition the S. G. P. T. was usually normal. The authors believe that S. G. P. T. and S. G. O. T. determinations are of diagnostic value in hepatic disease, particularly if interpreted critically in conjunction with other liver function tests.

Neonatal Tetanus.—Tompkins reported a high incidence of neonatal tetanus in Nigeria, where the cord is cut at birth with an unsterile stick or palm leaf and dressed with a variety of unsterile materials, including cow dung (*Brit. M. J.* 1:1382, 1958). In three years 141 patients with neonatal tetanus were treated at University College Hospital, Ibadan, with a mortality of 90%. The incidence of the disease was higher in the dry season than in the wet, probably because of the greater amount of dust. The length of the incubation period was closely related to the mortality, the mean incubation period of the survivors being 10.7 days and that of patients of the fatal cases 7.3 days. Mortality was also related to the interval between the failure of the infant to nurse, which was usually the first symptom, and the onset of tetanic spasms. The mortality was much higher if this period was less than 24 hours. The severity of the disease on admission was a useful, although not infallible, guide to the prognosis, the mortality being greater among those graded as severe.

No correlation was found between mortality and the dose of antitoxin, although there was a significantly longer survival time among those patients who received a dose of more than 20,000 units and who subsequently survived than among those who received less. Increasing the dose of antitoxin to 70,000 units did not lead to any further increase in survival time. It was therefore concluded that 50,000 units is sufficient. Sedation is an essential part of treatment, although Tompkins did not find that any one sedative was superior to any other. Sedation must be kept as light as possible to control spasms without depressing respiration. Feeding difficulties and respiratory complications in these infants were circumvented by withholding food by mouth and maintaining hydration and electrolyte

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The items in these letters are contributed by regular correspondents in the various foreign countries.

balance parenterally. Respiratory complications accounted for a number of deaths, some of which could have been prevented by tracheotomy.

Expectorants.—In the evaluation of expectorants many workers have studied their effect on the volume or weight of output of respiratory tract secretion, but Hillis and Stein (*Scottish M. J.* 3:252, 1958), stated that the effect on viscosity is more important than volume, because the ease with which sputum flows depends on its viscosity. Using a decrease in viscosity as an index of expectorant activity they examined several drugs used in cough medicines as expectorants. The sputum of patients with chronic bronchitis was collected over a five-day period, measured, and homogenized with sodium hydroxide solution, and its viscosity was index-measured by the time of fall in a capillary tube viscosimeter. The effect of potassium iodide, ammonium chloride, ipecacuanha, and a placebo on the volume and viscosity of sputum was then examined. The subjects tested served as their own controls. None of the drugs had any significant effect on the viscosity of the sputum, and only potassium iodide caused a significant increase in output.

Alcohol and Driving.—Alcohol as a cause of car accidents has been widely studied. Most of the investigations have been concerned with an examination of the effect of alcohol on reaction time and driving skill rather than on judgment and the assessment of risks while driving. Cohen and coworkers (*Brit. M. J.* 1:1348, 1958) believing that the latter is as important as driving skill as a factor in road accidents, carried out an investigation on Manchester bus drivers in their driving school to examine the effect of alcohol on road judgment and risk taking. After working an eight-hour shift the men had a meal and one to one and a half hours later were given either 2 oz. of Scotch whisky, containing 23 ml. of absolute alcohol, or three times this amount. The driver's task was to estimate how successful he would be in driving his bus between gaps of varying width marked by movable white posts. He was first asked if he thought he could do it, then he attempted to drive the bus through the gap. His performance was measured at different sizes of gap. It was found that drivers who took alcohol became involved in greater hazards than those who did not. As they consumed more alcohol their performance as well as their judgment progressively deteriorated, they were involved in greater hazards, and they displayed a false confidence in their driving abilities. Alcohol intensified any driver's tendency to overrate his ability in relation to his performance. Even small amounts of alcohol affected judgment and risk taking. The authors suggested that to reduce road accidents it should be an offense to take alcohol within a specified time before driving a car. Less than 0.5% of car accidents are attributed to alcohol by the police, but this is considered a gross underestimate, as they only prosecute in cases where the driver is obviously drunk.

Walls (*Brit. M. J.* 1:1442, 1958) examined the urine-alcohol concentrations of 312 persons arrested and charged with driving under the influence of alcohol. The figures were mostly distributed around a mean value of 300 mg. per 100 ml., which corresponds to a blood alcohol concentration of 230 mg. per 100 ml. According to Walls the decisions of the courts on driving offenses, in which the accused is charged with drunkenness, are not influenced at all by the legal evidence of urine-alcohol concentrations.

Medication and Anesthesia.—Dundee (*Brit. M. J.* 1:1433, 1958) called attention to the extent to which some drugs may influence the response of patients to anesthesitization. The side-effects of drugs taken for therapeutic purposes cannot always be predicted with certainty by pharmacologists, and sometimes they are only detected by chance many years after the preparation has been introduced. They may occur on the operating table or in the immediate postoperative period. Thus therapeutic agents whose main effect is to decrease vascular tone, such as the ganglionic blocking drugs or chlorpromazine, if given before an anesthetic, increases the hypotensive effect of narcotics, and severe and even fatal collapse may follow their administration before a normal dose of anesthetic. This applies particularly to the barbiturates given intravenously. Their hypotensive action is difficult to predict in certain patients. If they are given to patients receiving ganglionic blocking agents, the fall in blood pressure may be disastrous. Patients receiving other hypotensive agents such as the rauwolfia or veratrum alkaloids or mecamylamine may also react to anesthetics with a sudden and rapid fall in blood pressure. The phenothiazine derivatives used to control the tremor of paralysis agitans, such as caramiphen, and also some of the tranquilizers, prolong the narcotic action of anesthetics. They possess to a greater or lesser extent the same hazards as chlorpromazine. Such drugs also influence the effect of muscle relaxants. A dangerous degree of respiratory depression can result from the combination of analgesic drugs and the intravenously given barbiturates. A similar result can occur when cyclopropane is administered to patients who have had deep x-ray therapy to the head and neck.

Induced adrenocortical insufficiency, after the prolonged use of cortisone, its analogues, and corticotropin, makes patients sensitive to the stress of anesthesia and surgery. Prolonged severe hypotension, respiratory depression, and delayed recovery may follow operations on such patients. Catastrophes can be prevented by increasing the dose of steroid preoperatively, and if they do occur they respond to intravenously given hydrocortisone. Steroid-induced primary pituitary failure may persist for several months after therapy with the drugs is stopped. Dundee emphasized that during the preoperative period all patients should be questioned regarding steroid therapy. The hazards of inducing anesthesia in patients with a full stomach are now appreciated, and for this reason Dundee deprecated the preoperative preparation of diabetics with glucose by mouth. Other hazards that he encountered were the incompatability of oxytocin injection with light cyclopropane anesthesia, and the possibility of citrate intoxication, associated with an increase in venous pressure and the gradual onset of cardiac failure, as a cause of cardiovascular collapse after massive transfusion of stored blood.

John Snow Centenary.—The centenary of the death of John Snow, pioneer anesthesiologist, was celebrated in London in June by the laying of wreaths on his grave at Brompton Cemetery in London by the president and members of council of the Association of Anesthetists of Great Britain and Ireland, the dean of the Faculty of Anesthetists of the Royal College of Surgeons of England, and the presidents of the sections of anesthetics and epidemiology of the Royal Society of Medicine. John Snow administered chloroform to Queen Victoria in 1853 for the birth of Prince Leopold. Besides writing his classic work on the administration of chloroform and ether, he proved the water-borne spread of cholera in the epidemics of the disease that plagued London in his time.

Diamond Jubilee of Medical Corps.—The Royal Army Medical Corps celebrated its diamond jubilee this year. On June 23, 1898, Queen Victoria, who was then 80, granted it a royal warrant. At the time William Leishman, whose name is commemorated in the tropical disease leishmaniasis, was a young medical officer in the new Royal Army Medical Corps. He later became Lieutenant-General Sir William Leishman, Medical Director-General of the Army Medical Service, and professor of pathology of the Royal Army Medical College. Major-General Sir David Bruce, whose greatest contributions to medicine were his work in Uganda on sleeping sickness and undulant fever, which was subsequently named brucellosis after him, became commandant of the Royal Army Medical Corps College.

Drug Addiction.—There are 359 known drug addicts in Great Britain, according to the British government's report to the United Nations on narcotic drugs. Of these 70 are physicians, 15 are nurses, 2 are dentists, and one is a pharmacist. Female addicts outnumber male addicts by 11. The total number of 359 is an increase of 84 over the figure for the previous year. The commonest drug of addiction is morphine, with 149 addicts, followed by meperidine hydrochloride with 74, and heroin with 52. In the last year 95 prosecutions were brought for violation of the narcotic laws, and 90 of those prosecuted were convicted. There were 14 seizures of opium, the total amount weighing 5.3 kg., compared with 29, weighing 54.2 kg., in the previous year. More cannabis (marihuana), used mainly by Asians, Africans, and West Indians, was seized than in the previous year. There were 51 convictions for its unlawful possession, about 60% of the offenses occurring in London.

Public Blamed for High Drug Bill.—In a report of the committee appointed to investigate the cost of prescribing drugs under the National Health Service the public is blamed by implication, rather than the physician, for the big rise in the national drug bill. The committee, composed largely of physicians, was presided over by Sir Henry Hinchcliffe, a banker. In the last 10 years the cost of prescribing drugs has more than doubled. In 1949, the first full year of the health service, there were 202 million prescriptions, and last year there were 207 million. The increased cost is thus due to the cost of drugs and their compounding by the pharmacist, rather than to any great increase in the number of prescriptions issued. The cost has risen from $85,000,000 to $170,500,000, with a cost of 82 cents per prescription. The Hinchcliffe committee says that so far it has found no evidence of serious irresponsibility on the part of physicians in prescribing. The increase in drug cost was less than in other countries in Europe and the British Commonwealth with insurance systems.

The committee recommended (1) the production of a comprehensive prescription handbook, drawing the attention of medical schools to the National Formulary; (2) indication on the leaflets issued to physicians of the price of drugs; and (3) circulation to physicians of up-to-date prescribing statistics. It was suggested that before a new drug is put on the market it be given an approved name which should appear in advertising matter and on the drug package as prominently as the trade name. The report says that about 700 physicians, whose prescribing costs are much higher than the average, are visited each year. The president of the Association of the British Pharmaceutical Industry criticized the report on the grounds that it is a misconception that standard drugs are cheap and that proprietary preparations are not. Often proprietary preparations are actually cheaper. He also pointed out that vast sums are spent by the pharmaceutical industry on research and that the manufacturer can only recover the cost of research on a new drug by selling it under a proprietary name.

CORRESPONDENCE

WEIGHT REDUCTION

To the Editor:—In the Correspondence section of The Journal (166:2214 [April 26] 1958), Dr. A. R. Feinstein comes to the defense of the low-calorie, low-protein formula diet as used for weight reduction at the Rockefeller Institute. The diet contains 22 Gm. of protein, 52 Gm. of fat, 85 Gm. of carbohydrate and has a value of 896 calories (Feinstein and others, *Ann. Int. Med.* 48:330-343 [Feb.] 1958). No studies of nitrogen balance were made. Jolliffe (*J. A. M. A.* 161:1633-1636 [Aug. 25] 1956) showed most cogently that a decided negative nitrogen balance exists in obese individuals who are on such diets.

There is an important phase of this subject, namely, the caloric equivalent of body weight lost, which has not been explored at all by workers in this field. While fat can be stored in an almost pure state in the body, protein cannot be stored dry but retains with it three or more parts of water. Thus 1 Gm. of adipose tissue has a value of approximately 8 calories, while 1 Gm. of flesh has approximately a value of 1 calorie. In clinical weight reduction, when the patient is in nitrogen equilibrium, the caloric deficit is made up by the catabolism of fat. The caloric equivalent of 1 lb. of body weight lost is, under the circumstances, about 3,500 calories. In the Rockefeller formula diet, where a negative nitrogen balance is present, the caloric deficit is made up by the catabolism of fat and protein, and the caloric equivalent of 1 lb. of body weight lost is decidedly less. The proof of this is strikingly demonstrated in Benedict's study of the professional faster Levanzin (Benedict, F. G.: Study of Prolonged Fasting, publication 203, Carnegie Institution of Washington, 1915). Levanzin fasted for 31 days, during which time he lost 30 lb. Of the weight lost, 18.3 lb. (8319 Gm.) was flesh, of which 14 lb. (6,383 cc.) was water, and 3.7 lb. (1,664 Gm.) was protein with a value of 6,828 calories. If Levanzin had been in nitrogen equilibrium, the 6,828 calories would have been derived from adipose tissue with a loss of only 1.82 lb. of weight. The caloric equivalent of 1 lb. of body weight lost by Levanzin was 1,500 calories.

Feinstein further states: "In the outpatient studies, the percentages of weight loss in the formula-fed group were much higher than those obtained with many conventional diet programs." These two groups are not at all comparable. In the conventional groups the patient is in nitrogen equilibrium, and the caloric equivalent of 1 lb. of body weight lost is 3,500 calories. In the Rockefeller group, where a nitrogen deficit was present, considerable losses of water occurred, and the caloric equivalent of 1 lb. of body weight lost was decidedly less than 3,500 calories.

Most important of all is the fact that a considerable part of the weight loss which occurs when a negative nitrogen balance is present is spurious because it has no permanency. After the desired weight loss has occurred and the patient has been put on a diet adequate to maintain caloric equilibrium, the protein stores which have been depleted during the period of negative nitrogen balance will be replenished. For every pound of protein (1,850 calories) replenished, there will be retained 3 lb. of water, making for an increase of 4 lb. in body weight. Thus, even though the patient is in caloric equilibrium, he will continue to gain weight until the protein stores have been completely restored. If there have been large losses of protein, the gain in weight will be very large indeed. The conclusion can be drawn that a basic desideratum in the dietary management of obesity is the maintenance of nitrogen equilibrium.

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FETAL AND MATERNAL LOSS

To the Editor:—A paper on infant mortality by Verhoestraete and Puffer appeared in The Journal (167:950-959 [June 21] 1953). Some six years of work for the World Health Organization and the United Nations Children's Fund in rural China and northeastern Brazil gradually forced upon me a conviction that in so-called underdeveloped countries (i. e., countries with few machines and little money but many people), the quickest, simplest, and easiest approach to reduction of sickness and death at childbirth is by training rural midwives. One teaches them simply and practically to do a few things—the main ones being to (1) recognize easily perceptible anomalies of pregnancy early and, if possible, send women with such anomalies to a doctor before labor begins; (2) scrub their own hands with soap and hot, boiled, running water, poured from a tin can or kettle; (3) under no circumstances insert their fingers into the parturient's vagina; (4) use simple means of inducing respiration in apnëic newborn infant; and (5) keep the newborn infant, especially his navel, clean.

Experience in Chinese villages taught that thus-trained village midwives reduced deaths from infantile tetanus from 33% to zero by covering babies' navels with sterile gauze instead of plastering them with cow dung. This minimum may not be irreducible, but then, what is reducible in New York is not necessarily so in the Mexican Sierra Madre.

These training methods embody nothing new; they are ones that during World War II enabled the United States to run a completed Victory ship off the ways in 10 days, using, not skilled shipwrights and fitters, but raw, green laborers, who carried out only a few technical maneuvers, but these repeatedly and all day long.

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JOURNAL ARTICLE

To the Editor:—The undersigned greatly regret the omission of a crucial acknowledgment in their article, "Acute Blood Loss Requiring Fifty-eight Transfusions" (*J. A. M. A.* 167:985-986 [June 21] 1958). The patient was not treated in Cleveland Clinic Hospital, as might be inferred from the article. The patient was treated in St. Luke's Hospital, Cleveland, whose staff and facilities deserve full credit. The patient was a private patient of one of the authors (Taylor) and was seen by numerous consultants, one of whom was the senior author (Gardner).

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MISCELLANY

THE FUNCTIONS AND EDUCATION OF MEDICAL RECORD PERSONNEL

The American Association of Medical Record Librarians has acknowledged with gratitude the receipt of the report on "The Functions and Education of Medical Record Personnel" prepared for the Association by the Graduate School of Public Health, University of Pittsburgh, and approved the publication of the report by the University of Pittsburgh Press.

Although the association recognizes certain limitations in the survey relating to the practice of medical record keeping in various parts of the United States and the levels of medical record personnel, it believes the study well defines the basic medical record functions. It should be emphasized, however, that these various functions depend upon the needs of the individual hospital and the policies established by its administration.

One of the major functions assigned the medical record librarian is that of performing a qualitative analysis of the medical record. It is the opinion of the association that this responsibility must be clearly interpreted to mean that, while the medical record librarian is responsible for evaluating the quality of the record itself to insure internal consistency and completeness, this in no way implies a responsibility for evaluating the quality of medical care.

The association wishes to point out that, although it approves the collection of medical statistics as a proper function of the medical record librarian, it believes that the type of compilation should be frequently reevaluated to be certain that the data collected is meaningful and currently useful.

In light of the functions outlined in the report, the association believes that the philosophy of education recommended in the report should be thoroughly tested. It is the opinion of the association that, until such time as experience has clearly demonstrated the superiority of this program as an effective means of meeting the need for qualified personnel, the existing educational program in Medical Record Science should be continued and supported.

To implement the recommendations of the study, the American Association of Medical Record Librarians proposes to utilize its education consultant, education director, and Education and Registration Committee to develop a detailed sample curriculum along the lines proposed to submit to academic institutions interested in establishing medical record science programs. It is suggested that for purposes of evaluation this method of education be tried in a limited number of colleges or universities.

The proposed curriculum, however, varies radically in its approach to teaching medical record science from that currently being used in existing schools. To familiarize directors and instructors with all types of teaching methods and, also, to develop cooperatively more and better teaching materials, the association plans to expand its present program of workshops. It proposes, also, to recommend revision of the Essentials for an Acceptable School for Medical Record Librarians. As they stand, these essentials not only preclude the curriculum recommended by this study but they also conflict with the academic requirements of those colleges and universities which at the present time are affiliated with medical record librarian schools.

The association appreciates that the proposals so far discussed are long range in nature and cannot immediately meet the acute shortage of trained medical record personnel. Accordingly, it proposes an accelerated in-service training program for medical record personnel which will improve the skill of untrained workers but will in no way produce professional medical record librarians.

Statement of the American Association of Medical Record Librarians on the University of Pittsburgh's study entitled "The Functions and Education of Medical Record Personnel."

MEDICAL LITERATURE ABSTRACTS

PEDIATRICS

Intramedullary Transfusions in the Newborn Infant. S. Folena. Presse méd. 66:641-642 (April 12) 1958 (In French) [Paris].

Transfusions cannot always be given readily to the newborn infant by the intravenous route. Attempts to overcome this difficulty have led to the use of transosseous (intrafemoral and intrailiac) routes. The first or intrafemoral approach has proved especially valuable when transfusions are to be given to the premature infant. The second or intrailiac route, advocated by the author since 1945, seems to be more useful in the full-term newborn infant and in nurslings. Numerous investigations have shown that intrailiac transfusions are entirely comparable to those given intravenously. Not only can they be given without danger, but they also offer several advantages, notably ease of execution and an almost complete absence of the phenomena of shock.

Intrailiac transfusions must be given with a special needle, which has been devised by the author and which is quite similar to a trocar for sternal puncture. Its dimensions, for the newborn infant, should be 2 cm. in length and 1 mm. in diameter; it should be provided with a mandrel; and it must be sterilizable in a sterilizer. The puncture should be made in the bone 1.5 cm. behind the anterior-superior iliac spine and about 1 cm. below the superior margin of the iliac crest. The spongiosa in this region in newborn infants born at term is very abundant, and the cortex of the bone is especially thin, making it easy to penetrate the medullary cavity with the use of a light local anesthetic (ethyl chloride or, more simply, ether). Entrance into the medullary cavity of the iliac crest is virtually entrance into the venous system: hence, it provides a route for transfusion which is especially suited to use in the neonatal period.

Several infants with hemolytic disease have been successfully treated by this method. Blood was withdrawn, in infants needing exchange transfusions, from the radial artery while Rh-compatible blood was being given by the intrailiac route. Others, again, received only direct intramedullary transfusions (from the vein of the donor to the bone marrow of the infant, which the author considers preferable to the use of citrated blood). The following are the 3 other most important conditions in which the intrailiac route has been used to good effect: diarrhea of the newborn infant; sclerema, whose formerly high mortality has been enormously reduced by the practice of giving 1 or more intrailiac transfusions of compatible blood, as soon as the diagnosis has been made; and hemorrhagic disease. The advantages of this method of administering transfusions to the newborn infant are so great that it should be made known to all practitioners.

The Role of a Chronic Carrier in an Epidemic of Staphylococcal Disease in a Newborn Nursery. R. T. Smith. A. M. A. J. Dis. Child. 95:461-468 (May) 1958 [Chicago].

During the summer of 1956 an alarming number of infections in newborn infants and their mothers, both in the hospital and after discharge, occurred at a large general hospital in Minneapolis. Some of these infections were considered serious, but the majority were minor infections with serious potentialities. The hospital records of all newborn infants admitted to the nursery after May 1, 1956, were reviewed to determine the incidence of various infections in the nursery before the start of the epidemiologic studies. Physicians on the hospital staff who had delivered infants during the period were contacted to determine the incidence of infection in mothers and their infants up to 6 weeks after discharge. From the beginning of the investigation, all coagulase-positive staphylococci isolated were saved for bacteriophage typing. Staphylococcic infections developed in 117 of 981 infants, and breast abscesses developed in 24 mothers. In at least 3 families in which the mother or the infant had a clinical infection, staphylococcic disease also developed in another member or members of the family. Pyoderma, furunculosis, paronychia, sinusitis, and otitis media occurred in the siblings or in the fathers.

The highly virulent "epidemic" strain of staphylococcus, 42B/47C/44A/52/80/81, was isolated from a majority of the lesions cultured. The outbreak appears to have been originated and sustained by a chronically infected nurse who carried the epi-

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The place of publication of the periodicals appears in brackets preceding each abstract.

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demic strain and worked in both the delivery room and the nursery. Control of the outbreak resulted from removal of this person from the service, without the ancillary use of antibiotics or special skin care. Although tracing an epidemic outbreak to a single infected person, as was done here, may be unusual, this experience gives emphasis to the long-established significance of human infections or chronic carrier states as the prime course of hospital staphylococcic disease. The fact that a chronically infected carrier can be found working in the obstetric service of a modern hospital, unaware of the relationship of her difficulties to those of the nursery, attests to the importance of reeducation of personnel in the principles of aseptic technique and of an administrative policy which encourages reporting illness without fear of economic loss. A policy of giving nurses found to be chronic carriers of the epidemic strain a paid vacation during which they can undergo treatment should prove helpful.

Use of Combined Hormone and Mechlorethamine (Nitrogen Mustard) Therapy in Lipoid Nephrosis. C. D. West. A.M.A. J. Dis. Child. 95:498-515 (May) 1958 [Chicago].

This study extends previous observations on the combination of hormone and nitrogen mustard therapy in lipid nephrosis. Therapy employing a combination of a hormone and the nitrogen mustard, mechlorethamine hydrochloride, was given on 25 occasions to 12 children with lipid nephrosis. The disease had been present for more than 2½ months at the time that 22 of the courses of combined therapy were given. The effectiveness of the treatment was assessed by comparing the frequency of recurrence of the disease and responsiveness to hormone treatment before combined therapy with the course of the disease after combined therapy. The results strongly suggested that in children with pure lipid nephrosis the addition of mechlorethamine at the end of a course of corticotropin (ACTH), or of a steroid followed by corticotropin, results in 2 advantages, provided that the period of hormone administration prior to the institution of mechlorethamine treatment has been of sufficient duration.

These advantages are as follows: 1. Remission occurs with high frequency when mechlorethamine is given on the last 4 days of a course of hormone lasting 10 or more days. In all of 16 courses of combined therapy given while the disease was active, diuresis occurred coincident with the administration of mechlorethamine. With all except 2 courses, albuminuria likewise cleared. 2. Remission will be of greater duration than that observed after hormone therapy alone, provided that mechlorethamine administration is preceded by a treatment period with a hormone of at least 20 days' duration. Of 15 courses of therapy in which mechlorethamine administration was preceded by 20 or more days of hormone therapy during the previous 30 days, 13 were followed by a remission significantly longer than was observed with hormone therapy alone. The hormone used was either corticotropin or a steroid followed by corticotropin. Long remissions resulted whether, at the time of mechlorethamine administration, the disease was active, with albuminuria present, or in remission. Of 4 courses of therapy in which mechlorethamine administration was preceded by 15 to 17 days of corticotropin administration during the previous 30 days, 2 courses were followed by a long remission, and 2 appeared to have little influence on the course of the disease. Of 4 courses in which mechlorethamine administration was preceded by only 6 continuous days of corticotropin therapy, 3 failed to affect the duration of the subsequent remission, and 1 had a questionably salutary effect. It is felt that with the modified form of combined therapy now in use (long-term pretreatment with steroid followed by corticotropin) these results may be improved.

True Hermaphroditism: Report of a Case. W. Hughes, C. C. Erickson and W. Fleischmann. J. Pediat. 52:662-669 (May) 1958 [St. Louis].

The authors report a case of true hermaphroditism in a 15-year-old boy in whom at the time of birth it was noted that the external sex organs were ambiguous. Since they resembled those of a male more than those of a female, the infant was reared as a male. During his 13th year bilateral enlargement of the breast was noted, which continued to a size that caused him embarrassment. On physical examination, mammary ducts were palpated, radiating from the nipples of the breasts which were the size of those of an 18-year-old girl. A small amount of axillary hair was present. Pubic hair was present but did not extend onto the abdominal wall to a level that would permit the classification of male distribution. The phallus was 4 cm. in length, with a well-defined glans and a perineal hypospadias. A firm movable mass, 2 cm. in diameter, was palpable near the external inguinal ring in the right scrotal sac which resembled the labium majus. A defect in the left inguinal ring permitted a small herniation, but no gonad could be palpated in the left labium. No prostate or cervix could be palpated through the rectum. At endoscopy the apparent urinary meatus in the perineum was found to be a common channel, and about 2 cm. from the external orifice, there was a urethral orifice leading into a normal bladder. The channel extended posteriorly and superiorly into a blind pouch interpreted as a vagina. A biopsy section was removed from the labial mass, and microscopic examination identified the structure to be atrophic testicular tissue. Adjacent to the testicular mass in the right labium was a smaller elongated structure; histological study of the second mass proved this to be epididymis of essentially normal architecture. The hernial sac on the left side was opened, and the adjacent peritoneal cavity was explored with a finger. A small round mass was outlined, but its identity could not be established.

An exploratory laparotomy was performed and revealed a hypoplastic uterus, a grossly normal left fallopian tube, and a cystic ovary in the left adnexa, all of which were removed. Skin specimens from various portions of the body each revealed a male chromosomal pattern. Two months after the hysterectomy, a bilateral mammilliplasty was performed. Over an 8-month period, a 3-stage repair of the hypospadias was undertaken, producing a penile urethra. The vaginal cavity was not removed. No hormone therapy was deemed necessary. With testis on one side and ovary on the other, the case of the patient was classified as the lateral or alternating type, according to Hinman's simplified grouping of 3 types of true hermaphroditism. One can assume that serious psychological complications were avoided through rearing this patient consistently as a boy, leaving no doubt as to his assignment to the male sex. When his breasts started to enlarge, his gender role was already firmly imprinted.

Management of Bronchial Asthma in Children.

L. Unger, A. A. Wolf, J. H. Johnson and D. L. Unger. J. Pediat. 52:538-546 (May) 1958 [St. Louis].

True bronchial asthma is an allergic condition which is usually preceded or associated with seasonal or perennial rhinitis and with partial obstruction of the lower air passages. Bronchial asthma is characterized by wheezing, dyspnea, orthopnea, and cough. Demonstration of the causative allergens, especially in patients in whom asthma has begun after the age of 40 years, is not always possible; in children, however, the discovery of the allergen is almost always a comparatively simple matter. For example, in 1952, positive skin tests were obtained in 362 of 366 asthmatic children. A good history must concern itself not only with possible allergic factors but also with past illnesses, emotional problems, and details relating to previous immunizations. The physical examination must be thorough, with special attention to the lungs and heart as well as to the nasal passages. A complete blood count should be made in each case, as well as a Kahn test, a nasal smear, urinalysis, and determination of the erythrocyte sedimentation rate. Skin tests are indicated in almost all allergic conditions, but they are generally useless in urticaria and migraine. Tests may be negative in asthmatic infants and positive in the same children when repeated a few years later. Tests should be made with all possible inhalant materials and also with the foods the child eats. A proper allergy survey cannot always be made by performing 20 to 30 skin tests; in many children this number is insufficient, and the results will not be satisfactory. Tests should be made by the scratch method, but intradermal tests must follow if the scratch method does not yield adequate information. Physicians who perform only scratch tests can expect not more than 75% results; those who make only intradermal tests are also wrong, because (*a*) they are apt to bring on systemic reactions which may even be fatal, (*b*) they perform fewer tests and may therefore miss positive skin tests, and (*c*) intradermal tests are more painful.

Therapy may be specific, symptomatic, or preventive. The specific management of asthmatic children consists in avoidance of causative allergens, with or without hyposensitization; usually the results are good. Symptomatic therapy of bronchial asthma is nonspecific, and nothing more than temporary relief of symptoms can be expected. Reassurance is the most important single measure, especially if the child is having his first severe attack. For mild to moderate symptoms, repeated subcutaneous injections of 1:1,000 epinephrine in doses of 0.10 to 0.20 cc. usually suffice, along with 5 to 10 drops of a saturated solution of potassium iodide. If necessary, a mild sedative may be added, e. g., elixir of Benadryl. This combination is almost always effective. For more severe asthma, the epinephrine may be injected every 4 hours; often 0.10 cc. of Sus-Phrine, a long-acting epinephrine suspension, is added. Instillation of 5 grains of aminophylline rectally is helpful and is to be preferred to the use of aminophylline suppositories. In addition, sirup of ipecac will induce vomiting, and as the child vomits, he usually eliminates sputum which he has not yet learned to cough up. For the most severe cases (status asthmaticus), antibiotics, e. g., penicillin, should usually be added, because in almost all such cases there are infectious complications which cause the symptoms to continue. Corticotropin-gel and prednisone have become very important, but cortisone itself is rarely used any more. The corticosteroids are of great help in lessening asthmatic symptoms, but they are not without danger, and they do not cure asthma or any other disease.

Much can be done to prevent the development of allergic symptoms in children, especially children of allergic parents. The homes should be as free from dust and allergens as possible. New foods should be tried one at a time, at least a week apart, to see if symptoms occur. Children with a tendency toward asthma should be guided away from dusty occupations. Exposure to colds should be minimized. Psychosomatic factors, if present, should be given proper attention. If these precautions are carefully followed, the onset of severe asthma in children can be prevented, or, if asthma does occur, the symptoms can easily be controlled.

The Prevention of Bilirubin Encephalopathy. W. J. Waters. J. Pediat. 52:559-565 (May) 1958 [St. Louis].

Maternal titer values and/or a positive Coombs test by themselves are not an indication for replacement transfusion in hemolytic disease of the newborn due to Rh incompatibility. The main emphasis should be placed on the clinical condition and early course of the newborn infant, particularly the ability to handle bilirubin. A demonstrated rise of serum bilirubin toward critical levels (20 mg. per 100 cc.) early, particularly within 12 hours, remains the best single criterion for the need of replacement transfusion in questionable cases. Close supervision is essential. Clinical judgment, which requires a thorough understanding of the clinical and laboratory data, may indicate the necessity of transfusion in individual cases. Therefore, it is desirable to refer these infants to a medical center if adequate facilities and personnel are not available. The procedure itself is not without hazard, particularly in the hands of unskilled personnel. Replacement transfusions by present methods may be inadequate, in rare instances, to control the serum bilirubin level and prevent brain damage.

Accidental Digitalis Poisoning in Children: Report of a Case and Review of the Literature. C. C. Drevets. J. Pediat. 52:577-583 (May) 1958 [St. Louis].

Accidental drug poisoning in children is common and is becoming more frequent. Accidental digitalis poisoning, on the other hand, is very rare, especially in children. The present report concerns a 2-year-old boy who ingested about 1.5 mg. of digitoxin shortly after 8 a. m. on the day of admission to the hospital. He began to retch and vomit about noon and became seriously ill quite rapidly thereafter. He was lethargic and vomited repeatedly when examined in the emergency room at about 1 p. m. The heart rate was 96 and the rhythm was somewhat irregular. Serial electrocardiograms showed increasing signs of digitalis intoxication until the intravenous administration of fluids containing potassium was started. Several investigations have been made into the use of potassium in digitalis intoxication. Numerous workers have abolished various arrhythmias with potassium; about half succeeded when the arrhythmias were not due to digitalis, and almost all succeeded when they were due to digitalis. It has been suggested that potassium might inhibit the cardiac effects of digitalis. The intravenous use of potassium-containing fluids is attended with more danger than oral medication, but the persistent vomiting in this patient made intravenous administration necessary. The first infusion, given at a rate of 20 drops a minute, consisted of 500 cc. of 5% dextrose in water with 10 mEq. (750 mg.) of potassium chloride. The pulse rate became less irregular within 3 hours. Intravenous therapy was continued on the second day with 250 cc. of 2.5% dextrose in half-strength lactated Ringer's solution (39 mg. of potassium chloride). Later 250 cc. of 5% dextrose was given in 0.45% isotonic sodium chloride solution.

In this patient the use of an intravenous infusion not only afforded a vehicle in which to administer potassium ions, but it also helped to correct the fluid loss and electrolyte imbalance from the severe vomiting and cessation of fluid intake. It further helped to correct the acidosis of dehydration, which itself may cause potassium loss; and it helped to keep up an adequate urine volume to promote excretion of digitoxin and any excess of potassium which had been administered. Because of the persistent vomiting, the patient was also given 2 injections of 5 mg. of Thorazine 5½ hours apart, with fair results. At the end of the second day, when the child could retain fluids taken by mouth, he was given potassium chloride orally, 125 mg. every 4 hours. After 4 days of treatment no residual signs or symptoms were noted, and the patient was discharged. Although no definite conclusion can be reached concerning the value of potassium therapy, it appeared to have a beneficial effect on this patient, at least on the electrocardiographic signs of digitalis intoxication.

DERMATOLOGY

Hyperglobulinemic Purpura (Waldenström). O. Peterson. Nord. med. 59:562-563 (April 17) 1958 (In Danish) [Stockholm].

A case of Waldenström's hyperglobulinemic purpura in a girl, aged 15 years, is described. She is apparently the youngest patient with this disease to be reported on. There were pigmentations on the lower extremities after petechias, as well as slight enlargement of the spleen, increased sedimentation reaction, slight anemia, and positive formol-gel and thymol reaction. The electrophoresis curve resembled that in macroglobulinemia, but ultracentrifugation showed that the serum contained component S-7. The disease has a benign course but is of chronic character. No specific therapy is known, and treatment remains symptomatic.

The Senear-Usher Syndrome (Pemphigus Erythematodes): A Report of Eight Cases. V. M. Henington, B. Kennedy and P. R. Loria. South. M. J. 51:577-585 (May) 1958 [Birmingham, Ala.].

The authors report on 5 men and 3 women, between the ages of 27 and 66 years, with the disease which combines features of benign pemphigus and lupus erythematosus and which has come to be known as the Senear-Usher syndrome. The triad of lesions characteristic of the Senear-Usher syndrome was present in all 8 patients. These were flaccid bullae, crusting of the scalp suggestive of seborrheic dermatitis or even simulating psoriasis, and lesions of the butterfly area of the face suggestive of lupus erythematosus. It is significant that in 5 patients the lesions first appeared on the scalp. The oral lesions, which were present in a single patient, were apparently not related to the skin condition; they were transient and did not recur during the long duration of the illness. Although the facial lesions in the Senear-Usher syndrome usually consist of hard, infiltrated, scaly plaques that persist for weeks, they may take other forms. Sometimes the lesions have the appearance of seborrheic dermatitis; sometimes they are typical of lupus erythematosus. In the latter case the lesions occupy the butterfly area of the face, are discoid-shaped, and display carpet-tack scales. Unlike the typical lesions of lupus erythematosus, they may appear overnight and may disappear almost as rapidly. In this series the eruptions on the trunk began as small flaccid bullae which ruptured easily and were replaced by raw denuded patches or thick greasy crusts. Greasy crusted lesions occasionally simulated greasy seborrheic keratosis or impetiginous or psoriatic lesions. Blood studies were within normal range, except for an occasional slight anemia in 6 of the patients. Two patients had elevated leukocyte counts when the disease became acute and the bullae were filled with purulent fluid; these 2 patients presented a severe acute type of pemphigus vulgaris during part of their illness. The other 6 patients more properly fell into the pemphigus foliaceus group.

These observations support the general opinion that the Senear-Usher syndrome is a variant of pemphigus, perhaps an abortive pemphigus foliaceus, designated as pemphigus erythematosus. It shows acantholysis, but it does not present a distinct histological picture. Early lesions show acantholytic bullae in the superficial portion of the epidermis, usually in the stratum granulosum or just beneath it. Older lesions show acanthosis, papillomatosis, parakeratosis, and hyperkeratosis. Lesions of pemphigus erythematosus that develop into pemphigus vulgaris show the histological picture of the latter disease. If there is any clinical difficulty in differentiating lupus erythematosus from pemphigus erythematosus, the histological findings, the low leukocyte count, and the studies of the L. E. cells should resolve the problem.

The original outlook on the Senear-Usher syndrome complicated by pemphigus vulgaris has improved greatly since the advent of corticosteroid therapy. The 2 patients with the complication of pemphigus vulgaris and the 6 with the milder type of the disease responded well to treatment with corticotropin in the form of corticotropin-gel and prednisone (Meticorten). The patients were followed for more than 5½ years. Three of them did not require medication for periods varying from 1 to 4 years; the condition of the other 5 is satisfactory on small maintenance doses (20 units of corticotropin given intramuscularly for several weeks and 5 to 15 mg. of prednisone given by mouth daily).

Adrenocortical Dysfunction in the Early Stage of Pemphigus Vulgaris. H. A. Cohen, T. D. Ullmann and A. Dostrovsky. J. Invest. Dermat. 30:207-210 (April) 1958 [Baltimore].

Disturbances in water and salt metabolism have been described in pemphigus vulgaris, and a dysfunction of the adrenal cortex has been suggested by Talbott and others as the basic disturbance in this disease. More recently, the therapeutic effect of the adrenocorticotropic hormone and of the corticoids has again drawn attention to the possibility of a causal relationship between a disturbance of adrenocortical function and this disease. When the diagnosis of pemphigus vulgaris is made on the basis of the severe local and general manifestations, the disease has already caused such disturbances in the water and salt balance and in the general nutritive state that the adrenal cortical function must necessarily have altered considerably. Thus, a study concerning the possible relationship between underlying endocrinological disturbances and the disease should be based on early cases. The 13 patients with pemphigus in whom the authors examined the adrenocortical function were in the initial stage of the disease, the diagnosis having been confirmed by histological examination. Fourteen patients with skin lesions other than pemphigus served as controls. The tests performed on the pemphigus patients and on the controls were as follows: (1) the salt tolerance test before and after the administration of 10 mg. of desoxycorticosterone acetate; (2) the Robinson, Power, and Kepler test; (3) the 4-hour corticotropin test of Thorn; and (4) the 24-hour urinary excretion of 17-ketosteroids. The patients without pemphigus showed normal results in all the tests. The results in the pemphigus patients as a group were suggestive of the existence of adrenocortical dysfunction.

UROLOGY

Transition of Cystitis Glandularis to Primary Adenocarcinoma of the Bladder. J. L. Shaw, G. J. Gislason and J. E. Imbriglia. J. Urol. 79:815-822 (May) 1958 [Baltimore].

A 41-year-old woman was hospitalized with the chief complaint of an incisional hernia, dysuria, and cloudy urine. The urinary symptoms dated back 8 years to their first appearance after an abdominal operation for a benign gynecologic complaint. On hospitalization, physical examination showed a very obese woman with an incisional hernia in the midline of her lower abdomen, first-degree cystocele, and 2 plus pedal and pretibial edema. The urine showed many mucus shreds and 30 to 40 red blood cells per high-power field and was loaded with white blood cells. Aerobacter aerogenes and other coliform bacili were cultured. An intravenous urogram revealed good bilateral function with a morphologically normal upper urinary tract, but there was a large filling defect in the right side of the bladder. Cystoscopy revealed a large, broad-based, somewhat elevated tumor mass involving most of the right lateral wall of the bladder. Biopsy of tissue taken from the tumor revealed "polypoid masses lined by adenomatous glands which were mucus secreting in type; the diagnosis was cystitis glandularis (aberrant gastrointestinal tissue)." The tumor was removed by loop resection, and the base fulgurated. Pathological examination corroborated the diagnosis of cystitis glandularis.

When the patient returned to the clinic 22 months later, she complained of frequency, nocturia, and burning on voiding. Cystoscopy revealed a red, velvety mucosa with a mucoid exudate. Eight months later she was admitted to the hospital because of severe pain in her right hip. Cystoscopy and biopsy again showed cystitis glandularis. She returned intermittently during the next 7 months, during which time her bladder symptoms remained unchanged. The patient was then not seen until 5 years and 1 month from the time of the original biopsy and diagnosis of cystitis glandularis. Her complaints were frequency, nocturia, and, now, stress incontinence. Cystoscopy revealed an irregular. nonulcerated, hyperemic tumor involving most of the right lateral wall of the bladder. The clinical impression was that of carcinoma, and the patient was admitted for the 4th time. Transurethral biopsy was compared with previous biopsies and showed that the lesion had undergone malignant change and was a low-grade adenocarcinoma of the urinary bladder. There is a close relationship between cystitis glandularis, one of the common forms of proliferative cystitis, and primary mucus-secreting adenocarcinoma of the bladder. This relationship has been emphasized in the past but only on presumptive evidence based on the high incidence of the coexistence of these lesions and the similarities of theories of pathogenesis. The embryonic rest theory, the anatomic theory, and the theory of the metaplastic transposition of transitional epithelium to a glandular-type epithelium and adenocarcinoma are cited. The latter is the most widely accepted. To the authors' knowledge, this is the first report in which this change was actually observed and demonstrated in a patient. Proliferative cystitis is a premalignant lesion of the bladder, and it is urged that this fact be kept in mind in the clinical management of these forms of cystitis.

Malacoplakia: Review and Description of First Case in Denmark. R. Knoop. Ugesk. læger 120:498-504 (April 17) 1958 (In Danish) [Copenhagen].

Although malacoplakia resembles chronic cystitis, the characteristic plaque formation, dominating phagocytizing cells, and Michaelis-Gutmann bodies distinguish it from other diseases of the bladder. The case of malacoplakia reported is the 1st to be described in Denmark and apparently the 66th in the literature. The patient was a woman, aged 43 years, with a history of numerous attacks of grave cystitis during a 5-year period. Diagnosis was made by biopsy via cystoscopy. The patient had a healed Boeck's sarcoid in the lungs. Treatment with cortisone, antibiotics, indwelling catheter, and electrocoagulation has led to considerable improvement and possibly recovery. The diagnosis of malacoplakia can be established only by biopsy of tissue from the suspected area and microscopic demonstration of the typical cells and Michaelis-Gutmann bodies. Malacoplakia should be considered particularly in cases of long-continued, intractable cystitis. The prognosis in the individual case is difficult to evaluate. There is apparently a tendency to spontaneous recovery, but the course may be chronic, unaffected by therapy, and finally, often combined with severe chronic infection. In some cases with affected renal tissue, malacoplakia in itself can be fatal, with death from uremia. No etiological factor is known. There is no certain therapy. The disease may perhaps be a special form of Boeck's disease in the urinary tract.

THERAPEUTICS

The Treatment of Malignant Effusions with Radioactive Colloidal Gold (Au^{198}): A Review of Sixty-six Cases. S. H. Seal, S. Crosignani, G. Valvassori and others. Am. J. Obst. & Gynec. 75:1027-1033 (May) 1958 [St. Louis].

The authors report the results of 4 years' experience with the intracavitary administration of radioactive colloidal gold (Au^{198}) to 66 of 111 patients with malignant growths involving the pleural and peritoneal cavities, whose most important symptoms were due to fluid in the peritoneal or pleural cavities or both and who required frequent taps. Patients with ascites received doses varying from 150 to 225 mc. in the first injection, with an average of 175 mc. Patients who received pleural therapy were given a single dose ranging from 75 to 110 mc., with an average of 85 mc. The radiogold, which was diluted with a volume of 200 to 250 cc. of isotonic sodium chloride solution to ensure a proper distribution of the radioactive material in the cavity, was injected in accordance with the method of Rose and associates.

The palliative results in this study were analyzed in terms of the length of time required for the fluid to reaccumulate in the cavities. Good palliation was observed in 63.6% of the patients (no taps required for a period of at least 2 months after treatment); fair palliation was secured in 21.2% of the patients (no taps required for a period of 1 to 2 months); and no palliation was recorded in 15.1% of the patients (1 tap required less than 1 month after treatment, with reaccumulation of fluid in less than 2 months). No complications due to surgical trauma, local action of the radioactive gold, or infection were observed in any of the patients included in the survey. The usual side-effects of radiation therapy in the form of slight nausea and vomiting during the first 24 to 48 hours after the gold instillation were present in most of the patients. Blood studies performed before and after the treatment did not show any serious bone marrow depression. Approximately 70% of the patients experienced relief from the subjective symptoms. Although radioactive gold has an inhibitive effect on fluid formation, the injections seemed to have no detectable effect on the survival time.

Use of Phenylbutazone in Pulmonary Tuberculosis. I. De Gennaro and U. Massola. Minerva med. 49:813-818 (March 7) 1958 (In Italian) [Turin, Italy].

Phenylbutazone was administered to 21 patients with pulmonary tuberculosis, in whom relatively high febrile states had persisted despite the previous antibiotic therapy. Acute or subacute exudative type of the disease was present in 11 patients, and the chronic type accompanied by occasional attacks in 10. Phenylbutazone was given orally in daily tablet doses of 200 to 400 mg. before meals for a period ranging from a few days to 40 days. The best drug regimen seemed to consist in administering the drug in 1 or 2 divided daily doses in a few short courses of 5 to 7 days each. An immediate and prolonged improvement of the febrile state in all patients was the most beneficial effect observed even by using small doses of the drug. Amelioration of vegetative functions and a feeling of well-being, accompanied by partial or total remission of toxic symptoms, were also noted. Phenylbutazone was well tolerated by all patients, even in those instances where hemorrhagic episodes occurred. Gastric disorders took place only in severely dyspeptic patients, and this was corrected by decreasing the daily dosage. Hemorrhagic episodes developed in 3 patients, to whom the drug was given in a few short courses of 5 to 7 days with ample drug-free periods in between. Water retention developed in 1 patient. The authors believe that the antipyretic and antitoxic mechanism of phenylbutazone is comparable to that of the adrenals rather than the antipyretic drugs. Phenylbutazone can be used as a useful adjunct to other antituberculous drugs for the treatment of progressive, acute, subacute, or even chronic types of tuberculosis, where a prompt relief of fever is indicated.

Use of Orinase as a Basic Adjuvant in Management of Insulin-Dependent Diabetes. M. Fabrykant. Metabolism 7:213-221 (May) 1958 [New York].

Thirty-eight patients with stable diabetes mellitus and 12 patients with labile diabetes mellitus were given tolbutamide (Orinase) as a supplement to insulin therapy for periods of up to 20 months. Ten of the 38 patients had mild disease and were between the ages of 39 and 75 years at the onset of the disease; 22 patients had moderately severe disease and were between the ages of 34 and 56 years at the onset of their disease; and 6 patients had moderately severe disease and were between the ages of 11½ and 17 years at the onset of their disease. Of the 12 patients with labile disease, 7 were over 20 years of age and 5 were aged less than 20 years at the onset of their disease. Eight of the patients with stable diabetes who had cardiovascular complications and 10 of the patients with labile diabetes were hospitalized when tolbutamide therapy was instituted. Combined tolbutamide-insulin therapy was started with the remaining 32 patients when they were made ambulant. Combined tolbutamide-insulin therapy can be given to nonhospitalized patients with stable and labile diabetes, but initial hospitalization is recommended for patients with cardiovascular disease.

Beneficial effects from combined tolbutamide-insulin therapy, which could not be obtained by administration of insulin alone, were observed in 28 patients with stable diabetes and in 9 patients with labile diabetes. These benefits consisted in a 10 to 70% decrease of insulin requirement in the patients with stable diabetes and in a 10 to 50% decrease in the patients with labile diabetes, an easier regulation and stabilization of the diabetes, and an increased feeling of well-being. Therapeutic failures of this combined therapy were observed in 10 patients with stable diabetes and 3 patients with labile diabetes. Among the 10 patients with stable diabetes were the 6 who were less than 17 years old at the onset of their disease, and the other 4, who were adults at the onset of their disease, had a high insulin requirement of up to 116 units daily. Of the 3 patients with labile disease, 2 plunged into ketosis and required large additional doses of insulin to restore control; the third, a 6-year-old boy, reacted with paradoxical hyperglycemia and increased glycosuria when he was given tolbutamide without decreasing his insulin dose. In some patients with stable mild diabetes, an early favorable response to tolbutamide, which seemed to indicate that it might serve as a complete replacement for insulin, proved to be only temporary within 2 or 3 months of treatment. In some patients with stable mild diabetes and a high insulin requirement, and in those with labile diabetes, an initial resistance to tolbutamide therapy was followed by a remarkable improvement with its continuous use. In the light of present experience, forecasts of responsiveness based on tolbutamide loading tests or on short-term experiments may be misleading. The use of tolbutamide is an individual experiment in each case. In 6 patients with angina pectoris, a striking relief of anginal complaints coincided with the institution of tolbutamide therapy. These observations suggest a possible relationship between the employment of tolbutamide and the improvement in anginal pain, but corroboration of this relationship must await more extensive and especially designed studies.

PATHOLOGY

Considerations on Changes of the Serum Lactic Dehydrogenase Activity in the Course of Various Pathological States. L. Contro. Minerva med. 49: 731-733 (Feb. 28) 1958 (In Italian) [Turin, Italy].

The elevation of serum lactic dehydrogenase activity has been observed in association with certain neoplastic and nonneoplastic diseases. The author tested the serum level of lactic dehydrogenase activity of more than 200 unselected hospitalized patients. Relationships between serum levels of lactic dehydrogenase activity and glutamic oxaloacetic transaminase activity in patients with myocardial infarction, as well as between serum levels of lactic dehydrogenase activity and bilirubin activity in patients with acute hepatitis, were also studied. The highest serum lactic dehydrogenase activity levels, in descending order of magnitude, were observed in patients with the following diseases: neoplasms, myocardial infarction, acute hepatitis, and cardiac decompensation. Serum values were within normal limits in patients with chronic liver disease and rheumatic disease. Release of enzyme into the blood stream in neoplastic disease may be caused by cellular lysis, by membranous chemophysical changes, or by changes of metabolic order.

Variations of serum levels of lactic dehydrogenase activity and glutamic oxaloacetic transaminase activity in patients with myocardial infarction were inconsistent during the first 5 to 10 days of disease; in some patients the serum levels of the 2 enzymes reached the peak value and decreased at the same rate throughout the period of observation, whereas in others the lactic dehydrogenase activity level reached its peak value when the glutamic oxaloacetic transaminase activity level was already descending. Correlation between serum levels of lactic dehydrogenase activity and bilirubin activity in patients with acute hepatitis was consistent; the levels increased and decreased at a close rate during the first 45 days of the disease.

The Relationship Between the Clinical and the Histological Features of Acute Glomerular Nephritis: Based on a Study of Renal Biopsy Material. M. S. R. Hutt, J. L. Pinniger and H. E. de Wardener. Quart. J. Med. 27:265-291 (April) 1958 [Oxford, England].

The authors report on renal biopsy findings in 15 patients with a clinical diagnosis of acute glomerular nephritis and compare the clinical features with the extent of the structural changes observed. Patients whose initial clinical features were similar to those of acute glomerular nephritis, but who were proved subsequently to be suffering from some other disease, were not included. Clinically, 14 of the patients could be divided into 2 groups, depending on the presence or absence of persistent proteinuria (that is, proteinuria each day for the first few days after admission). The 15th patient is considered separately, for, although this 35-year-old man suffered from a typical attack of acute glomerular nephritis with hematuria, hypertension, and cardiac failure, the renal biopsy was not performed until 6 weeks later, when he had recovered completely except for the continued presence of proteinuria. All the patients in this series were alive and symptomless 1 year after their attack of acute glomerular nephritis.

These patients had only minor changes in the epithelium of Bowman's capsule. Clinically, these patients had edema and cardiac failure without proteinuria, hematuria, or hypertension. Eleven patients showed extensive abnormalities in the glomerular tufts. These lesions consisted of varying degrees of nuclear proliferation, infiltration of polymorphonuclear leukocytes, and increase of eosinophilic internuclear material. Six of these patients also had focal areas of severe tubular degeneration and inflammatory cell infiltration of the interstitial tissue. Microscopic lesions of the glomerular tufts were always associated with proteinuria and usually with hematuria; the blood pressure, blood urea level, and creatinine clearance were also related to these structural changes, though not with such consistency. Two patients had severe impairment in the ability to concentrate the urine; both had multiple tubular lesions. An erythrocyte sedimentation rate greater than 55 mm. in 1 hour was associated with widespread renal damage with interstitial and tubular lesions. Only 2 patients had proteinuria for more than a year; in addition to glomerular changes, both had numerous tubular lesions.

QUESTIONS AND ANSWERS

PAIN FROM INTERSTITIALLY APPLIED RADIUM NEEDLES

To the Editor:—*Please suggest treatment for severe pain due to radium needles which were applied interstitially seven months ago for treatment of an epidermoid cancer. The cancer was located on the soft palate of a 70-year-old man. The area around the cancer area is red and inflamed, but the cancer itself is healed. A pathologist reported that clippings from the throat were negative. The patient is able to eat if he dissolves two or three aspirin tablets in his mouth.* *M.D., South Carolina.*

Answer.—In this consultant's experience, interstitial application of radium needles to the soft palate has been a very frequent cause of severe pain. Such pain is often associated with impending radiation necrosis in tissue. There is no one specific treatment for this disability. The aspirin treatment described is excellent. In many instances narcotics are required. Copious irrigations with a mild saline solution three or four times a day will be of help. Penicillin injected intramuscularly may help to control or shorten the process. In some cases, surgical excision of the soft palate may give the only relief. Nutrition is exceedingly important under these conditions. A liquid diet, given by way of a soft rubber catheter inserted through the nostril, may obviate some of the discomfort in eating.

ASTHMA AND PNEUMONIA

To the Editor:—*Are asthmatic persons immune to pneumonia? The patients referred to have never coughed, have no Laennec's pearls, but do suffer, complaining that they feel their chests to be as in a vise when they are outside in temperature below 40 F. They are comfortable indoors. They have no coryza and no cardiac symptoms.*

H. Grosby, M.D., St. Louis, Mo.

Answer.—Asthmatic persons are not immune to pneumonia. Asthma is most simply defined as a symptom complex, consisting of shortness of breath with characteristic wheezing associated with interference with the free flow of air through the lumen of the bronchi, usually due to spasm of the bronchial musculature, edema of the bronchial mucosa, and accumulation of thick, tenacious sputum in the lumen of the bronchial tree. Any one of these elements may be present without the other two. Since many conditions may produce this pathological picture, there are many causes of asthma. Among them might be mentioned allergy, infection, tumor, emphysema, endotracheal tuberculosis, and cardiac failure. In young children, bronchiolitis, often with associated collateral pneumonitis, may produce symptoms of asthma. Cough is frequently, but not always or necessarily, associated with asthma. It is usually provoked by the presence of thick tenacious secretions and represents an effort on the part of the patient to expel the material. Components of this bronchial secretion which are often described with the eponyms, Laennec's pearls, Charcot-Leyden Crystals, and Curschmann's Spirals, are not at all necessary to make a diagnosis of asthma. Coryza is present only if the patients have, in addition to asthma, a concomitant allergic or infectious rhinitis. Patients with mild cases of asthma often complain of heaviness on the chest. Outside cold weather below 40 F may trigger or bring on such an attack of asthma, which is relieved when the patient enters a warm room. Such mechanisms of inducing symptoms of asthma are usually nonspecific and include exertion, sudden laughter, and undue emotional stress. The best diagnostic finding in the symptom complex of asthma is the objective one of the presence of dry rales in the chest, most pronounced on expiration. Having ruled out angina pectoris, the questioner may assume this diagnosis of asthma in his patients if, on auscultation of the chest, he finds these characteristic rales.

PHYSIOLOGICAL CHANGES AFTER HYSTERECTOMY

To the Editor:—*What would be the physiological changes following a hysterectomy before menopause in a nulliparous woman? Does the estrogen cycle continue exactly as before, with the possibility of premenstrual tension, breast changes, and other factors? How do the severity and time of onset of menopausal-signs and symptoms compare with what might have occurred had not the uterus been removed?*

M.D., Saskatchewan, Canada.

Answer.—Amenorrhea is the principal physiological change following a total hysterectomy. If a subtotal hysterectomy is done, periodic menstrual bleeding of some degree may persist. Aside from

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

these factors, there is no evidence that total hysterectomy results in hypo-ovaria or hyperovaria. Premenstrual tension, painful breasts, and other signs which have been present before surgery will frequently disappear after hysterectomy. On the other hand weight gain, retention of fluid, and painful breasts may first occur after a hysterectomy. Although the idea is prevalent that the menopause occurs soon after hysterectomy because of curtailment of some of the blood supply to the ovary, there is no scientific evidence to prove it. Being cognizant that the menopause may occur between the ages of 30 and 52, one can understand how the menopause may happen almost simultaneously with the removal of the uterus. It has been shown beyond a doubt that ovarian activity may go on for a long period after a physiological menopause or after amenorrhea is brought on surgically. The uninformed patient may connect the hysterectomy with the menopause because of the absence of menstruation.

EMULSIFYING AGENTS AND WEIGHT GAIN

To the Editor:—*Have detergents, such as polysorbate 80 or pancreatin, any place in the management of postgastrectomy (dumping) syndrome? The patient in mind had a subtotal resection with gastrojejunostomy, and she now has a mild dumping syndrome and diarrhea one to three days a week. Despite a good intake of calories, she cannot be made to gain weight, even with the use of such steroids as norethandrolone. Antispasmodics have been tried.*

M.D., California.

Answer.—Factors leading to development of the dumping syndrome are not well understood; both organic and psychological causes have been implicated. It is unlikely that defective handling of fat accounts for the postprandial weakness, diarrhea, and other features which are commonly observed in this condition. Therefore, administration of emulsifying agents or of pancreatic extract would not be expected to effect improvement of these symptoms. So far as loss of weight is concerned, it seems clear that excretion of an abnormal quantity of fat in the feces might contribute to this symptom. Some reports have indicated that administration of emulsifying agents or of a combination of pancreatic extract and bile salts (but not pancreatic extract alone) may lead to partial correction of this defect. Thus far, however, results usually have been inconclusive and the value of these agents in treatment not proved. If the patient can be encouraged to take an extra 500 calories of food each day and to avoid the use of fluids at mealtime, nutrition may be, as it often has been, improved by these measures alone.

HYPNOSIS IN DERMATOLOGY

To the Editor:—*A patient has inquired regarding the possible use of hypnotism in a severe, chronic, long-standing bullous type of eczema. There have been articles on its use in most other fields, but none have been seen in dermatology. Please give information on its use in this field.*

C. D. Klaus, M.D., Iron Mountain, Mich.

Answer.—The use of hypnosis in dermatology has been reported in the literature for some years. Several of the recent books on dermatology have emphasized the emotional factors in skin conditions, especially in eczema. Gordon (Foreign Letters, *J. A. M. A.* **158**:1458 [Aug. 20] 1955) reported the use of hypnosis in a patient with dermatitis herpetiformis of 10 years' duration. The lesions cleared rapidly under hypnosis and remained so after a two-year follow-up. Any psychiatrist in America who has used hypnosis has undoubtedly found it effective in such cases. The following references are worthy of note.

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Sneddon, I. B.: Mind and Skin, Brit. M. J. **1**:472-475 (March 19) 1949.

Horan, J. S.: Management of Neurodermatitis by Hypnotic Suggestion, Brit. J. M. Hyp. **2**:43, 1950.

Kline, M. V.: Delimited Hypnotherapy: Acceptance of Resistance in Treatment of Long Standing Neurodermatitis with Sensory-Imagery Technique, J. Clin. & Exper. Hyp. **1**:18, 1953.

Stokvis, B.: Application of Hypnosis in Organic Diseases, J. Clin. Exper. Hyp. **4**:79, 1956.

REMOVAL OF VOCAL CORD POLYPS

To the Editor:—*What causes polyps to grow on the vocal cords in young children? Should they be removed as soon as diagnosed or when they begin to cause respiratory distress? How often do they recur, and what is the best method of removal to prevent their recurrence?*

M.D., Georgia.

Answer.—Polyps and polypoid chorditis occur much more rarely in young children than in adults. There is no great urgency in their removal if they are not obstructive, but the best method of removal is superficial stripping of the cords under direct laryngoscopy. It is absolutely necessary to avoid trauma to the underlying tissues of the cord if a good ultimate voice is to be obtained. Allergy may be a factor in these cases, and attention to the allergic indications is most important.

WASHINGTON • NEWS

FROM THE WASHINGTON OFFICE OF THE AMERICAN MEDICAL ASSOCIATION

Review of Bills Enacted as Adjournment Time Nears . .

AMA Asks Support for White House Session on Aging . .

Senate Vote on Technicality Sidetracks Keogh Bill . .

PHS Renews Plea for Poliomyelitis Vaccine Use . .

TEN HEALTH-MEDICAL BILLS PASSED AS ADJOURNMENT RUSH OPENS

At least 10 bills of direct or indirect interest to medicine had been passed by the 85th Congress as it moved into what were expected to be the final days of its closing session. Half a dozen others were hanging in the balance, passed by both chambers and waiting conference committee decision or passed by one house and waiting final action in the other.

Of greatest importance, a social security bill was sent on its way without the Forand proposal for hospitalization of the aged. This idea, strongly opposed by the American Medical Association and most other groups in the health-medical fields, will be an important issue in the new 86th Congress which meets in January.

Medicare was continued, although in restricted form, after a controversy that lasted all the way to the conference committee. After the House had imposed restrictions that would have virtually wrecked the civilian program, Senator Knowland succeeded in getting the damage repaired on the Senate floor. The Senate's action then was sustained by the conference committee, which, however, instructed the Defense Department to channel a great many more of its dependents to service hospitals.

On another military bill, for reorganizing the Defense Department, Congress voted for a plan that would allow elimination of the post of Assistant Secretary for health and medical matters, action the department was preparing to take. However, efforts are continuing to induce the department to preserve this high-level medical post, which the A. M. A. and other health-medical organizations had worked to have established. Whether the department will change its policy is not known at this time.

A new record was set in the health budget for the Department of Health, Education, and Welfare, with the National Institutes of Health particularly favored by Congress. They received a total of 294 million dollars, the cancer institute topping the list at 75 million.

The Hill-Burton hospital construction program also fared well, receiving more money than Congress had ever before allocated to it—186 million dollars. Also, the program was extended five years beyond its scheduled expiration date of July 1, 1959, and was amended to allow applicants who object to federal grants to receive instead long-term, low-interest loans.

Another program—for matching construction grants for building medical research facilities—also was extended, but an effort to amend it to allow the money to be used also for teaching facilities failed when it was decided that the change might lead to a controversy that would endanger passage of the simple extension bill. Under this arrangement 30 million dollars a year is distributed to medical schools, hospitals, and laboratories.

While medical schools were denied construction help, Congress did vote to give financial assistance to the country's schools of public health. Here the argument was that the schools educate doctors and others for service not in a particular state or region but for public health work in this country and some foreign countries and that therefore the federal government owes them something. The authorization is one million dollars a year.

In separate bills, pay increases were voted for the Veterans Administration's medical personnel and for military physicians (as part of a general military pay increase bill). A provision in the VA bill that would have up-graded optometrists to the same salary and status as physicians was eliminated after protests from the A. M. A. and other groups.

Of concern to many physicians, a bill was passed for federal assistance to states to help them set up effective civil defense organizations. It was touch-and-go for several other bills.

After receiving an overwhelming vote of approval in the House, the Keogh bill to allow the self-employed to defer income tax payments on money put into retirement funds encountered trouble in the Senate.

A bill for federal guarantee of mortgages for proprietary nursing homes (through FHA) passed the Senate late in the session but was stalled in the House Rules Committee. However, the possibility remained that it would be lost through inaction on the part of the House. The measure had the support of the A. M. A., as part of its long-range program of solving the health problems of the aged.

Another A. M. A.-supported bill looking toward solution of some of the problems of older citizens—one calling for a White House Conference on aging—cleared the House and the Senate Labor and Welfare Committee and needed only Senate approval.

Two other bills with medical implications stood some chance of enactment—or at least their fate wouldn't be decided until the hour of adjournment. Both Senate and House had passed measures requiring union, management, and joint welfare funds to publicize and report on their activities. However, the versions were different and there was the possibility that the conference would not have time to work out a compromise acceptable to both chambers. A bill to give the United States greater control over chemical additives to foods passed the House, but its fate in the Senate was uncertain, mostly due to the shortage of time.

(Continued on next page)

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Lown, B., and Levine, S. A.: Current Concepts in Digitalis Therapy, Boston, Little, Brown & Company, 1954, p. 23, par. 2.

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A. M. A. ASKS RECONSIDERATION OF BILL ON AGING

The American Medical Association made a strong plea to the Senate Labor and Public Welfare Committee for reconsideration of the stalled bill for a White House Conference on the Aging. Shortly thereafter, the committee, which originally voted to postpone indefinitely any action on the House-approved bill, proceeded to vote it favorably to the Senate.

In a letter to Chairman Lister Hill and all members of the Committee, Dr. F. J. L. Blasingame, A. M. A. executive vice-president, stated that the association was "distressed" to learn about the postponement of action. He urged reconsideration.

Dr. Blasingame said that the A. M. A. has had a deep and long-standing interest in the problems of the aged, especially in regard to their health needs. The A. M. A.'s Committee on Aging recently has held regional conferences in Seattle, Dallas, Philadelphia, Birmingham, and Omaha. Dr. Blasingame then pointed out that the association has called a national conference on aging in Chicago, Sept. 12-14. About 30 state medical societies have created committees on aging, and by September 40 such committees are expected to exist.

The Senate committee amended the bill to provide that the White House Conference be called in January, 1961, instead of September, 1960, and reduced the authorized appropriation.

KEOGH BILL SIDETRACKED BY SENATE VOTE AS NOT GERMANE

By a 52 to 32 vote, the Senate on Aug. 12 decided that the Keogh retirement bill was "not germane" as an amendment to another taxation bill, a technical development that virtually ended all possibility of enactment of the Keogh measure before adjournment.

The bill, long a goal of the American Medical Association and most other groups representing the self-employed, would permit deferment of U.S income taxes on a part of the income of self-employed if the money were placed in a retirement fund. Maximum annual setaside would be $2,500 and maximum lifetime setaside, $50,000.

Despite the legislative setback, the Keogh bill made more progress in this session than ever before. It passed the House by an overwhelming vote. Its sponsors, led by the American Thrift Assembly, are prepared to renew efforts for passage when the next Congress meets in January.

In the Senate, the situation developed this way: When a measure containing numerous technical amendments to tax laws came up for debate, Sen. Charles E. Potter (R., Mich.) moved that the Keogh bill be made an amendment. Ensuing debate brought out that the Treasury Department estimated that the bill would mean a revenue loss of 365 million dollars. (Sponsors of the bill say that is far too high.) Also, a point was made that the Senate Finance Committee had not yet held hearings on the Keogh plan.

Before a vote could be taken on the Keogh amendment, Sen. Wayne Morse (D., Ore.) proposed a substitute motion that carried an annual limit of $1,000, but with all taxpayers, employed and self-employed, eligible for the benefits. Senator

Morse, saying the tax loss might be as high as 1.9 billion dollars, explained that he was after "uniform justice," that the Potter amendment was discriminatory, and that his amendment would be adopted or none would.

The vote came about when Sen. Robert S. Kerr (D., Okla.) inquired if the Potter amendment were germane to the bill it would amend. On advice of the Senate parliamentarian, the ruling was that it was germane and could be considered. Senator Kerr then, on a point of order, appealed for a vote to reverse the ruling as to both the Potter and Morse amendments.

The roll call vote resulted in reversal of the chair, automatically ending consideration of both amendments.

Senator Potter led the unsuccessful fight for his amendment through the long debate, when he received support from a number of others, including Senators Bricker, Javits, and Neuberger. Those speaking against the Potter amendment included Senators Long (who argued extensively), Bush, Martin of Pennsylvania, Lausche, Williams, and Morse.

SURGEON GENERAL URGES MORE USE OF SALK POLIOMYELITIS VACCINE

With the peak poliomyelitis months at hand, Surgeon Gen. Burney has issued a new warning to the 40 million Americans under 40 years of age who have not yet had Salk vaccine shots.

The Public Health Service estimates that about 50 million in the susceptible under-40 age group have had at least three shots and that about 20 million have had one or two. The PHS recommends two shots within a month and a third at least seven months later but points out that the third is highly effective even if given two or three years after the initial injections.

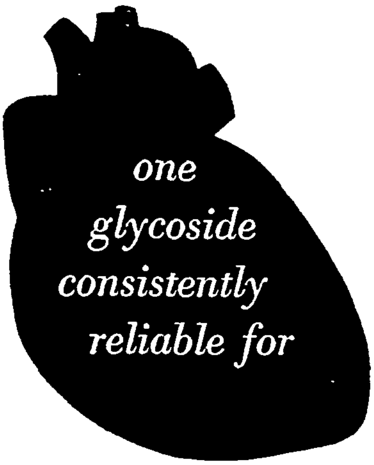
Dr. Burney cautioned that this may turn out to be a "high incidence" year for poliomyelitis, as during the third week in July the cases reported raised that week's total higher than for the comparable week in 1957 for the first time this year.

Dr. Burney said in part:

"Even before the development of the vaccine, there were years when the incidence of poliomyelitis was naturally low. We know that 1956 and 1957 were such years because there was relatively little poliomyelitis among the unvaccinated portion of the population. Should 1958 prove to be a year of natural high incidence, it is possible that there will be many cases among the 55% of the population under 40 who are not fully vaccinated.

"For maximum protection the full series of three shots is needed. Physicians in practice and in health departments are urged to make every effort to provide the full course of three injections.

"While the Public Health Service has recommended a series of three shots on a mass basis as a public health measure to give high levels of protection to the greatest number, physicians in individual cases may well recommend and parents may wish a fourth or booster injection of vaccine to be given a year or more after the series of three. This added protection will be particularly important in individuals living in or going to high incidence areas or where other personal factors make the greatest margin of safety desirable."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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice President.

1958 Clinical Meeting, Minneapolis, Dec. 2-5.

1959 Annual Meeting, Atlantic City, June 8-12.

1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.

AMERICAN

August

American Congress of Physical Medicine and Rehabilitation, Philadelphia, Bellevue-Stratford Hotel, Aug. 24-29. Dr. Frances Baker, 1 Tilton Ave., San Mateo, Calif., Secretary.

Northwest Proctologic Society, Sun Valley, Ida., Aug. 27-29. Dr. John McKay, 615 Medical Dental Bldg., Seattle, Secretary.

Public Relations Institute, Drake Hotel, Chicago, Aug. 27-28. Mr. Leo Brown, 535 N. Dearborn St., Chicago 10, Director.

September

American Academy for Cerebral Palsy, Sheraton-Biltmore Hotel, Providence, R. I., Sept. 25-27. Dr. Raymond R. Rembolt, University Hospitals, Iowa City, Ia., Secretary.

American Association of Obstetricians and Gynecologists, The Homestead, Hot Springs, Va., Sept. 4-6. Dr. E. Stewart Taylor, 4200 E. 9th Ave., Denver 20, Secretary.

American College of Physicians, Mid-West Regional Meeting, Milwaukee, Wis., Sept. 27. Dr. James F. Gleason, 7 S. Oxford Ave., Atlantic City, N. J., General Chairman.

American Fracture Association, Shirvin Hotel, Oklahoma City, Okla., Sept. 29-Oct. 4. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Secretary.

American Medical Writers' Association, Hotel Morrison, Chicago, Sept. 26-27. Dr. Harold Swanberg, 510 Maine St., Quincy, Ill., Secretary.

American Roentgen Ray Society, Shoreham Hotel, Washington, D. C., Sept. 27-Oct. 3. Dr. C. Allen Good, 200, 1st St., S. W., Rochester, Minn., Secretary.

Colorado State Medical Society, Broadmoor Hotel, Colorado Springs, Sept. 24-27. Mr. Harvey T. Sethman, 1612 Tremont Place, Denver 2, Executive Secretary.

Kansas City Southwest Clinical Society, Municipal Auditorium, Kansas City, Mo., Sept. 22-25. Mr. A. L. Bingham, 3036 Gillham Rd., Kansas City 8, Mo., Executive Secretary.

Kentucky State Medical Association, Brown Hotel, Louisville, Sept. 23-25. Mr. J. P. Sanford, 1169 Eastern Parkway, Louisville 17, Executive Secretary.

Michigan State Medical Society, Sheraton-Cadillac Hotel, Detroit, Sept. 30-Oct. 3. Dr. L. Fernald Foster, 606 Townsend St., P. O. Box 539, Lansing, Mich., Secretary.

Mississippi Valley Medical Society, Morrison Hotel, Chicago, Sept. 24-26. Dr. Harold Swanberg, 510 Main St., Quincy, Ill., Secretary.

Montana Medical Association, Northern Hotel, Billings, Sept. 11-13. Mr. L. R. Hegland, P. O. Box 1692, Billings, Executive Secretary.

Nevada State Medical Association, Elko, Sept. 17-20. Mr. Nelson B. Neff, P. O. Box 188, Reno, Executive Secretary.

New Hampshire Medical Society, Mt. Washington Hotel, Bretton Woods, Sept. 19-22. Mr. Hamilton S. Putnam, 18 School St., Concord, Executive Secretary.

Northeastern Section, American Urological Association, Equinox House, Manchester, Vt., Sept. 12-13. Dr. F. O. Harbach, 831 James St., Syracuse, N. Y., Secretary.

Oregon State Medical Society, Columbia Athletic Club, Portland, Sept. 3-5. Dr. Max H. Parrott, 1020 S. W. Taylor St., Portland 5, Secretary.

Tennessee Valley Medical Assembly, Read House, Chattanooga, Tenn., Sept. 29-30. Dr. Harry A. Stone, 109 Medical Arts Bldg., Chattanooga 2, Tenn., Secretary.

Texas Academy of General Practice, San Antonio, Tex., Sept. 22-24. Mr. Donald C. Jackson, 1905 N. Lamar, Austin, Tex., Executive Secretary.

Tri-State Medical Society, Shreveport, La., Sept. 18. Dr. J. C. Sanders, Sanders Clinic, Kings Highway, Shreveport, La., Secretary.

Utah State Medical Association, Hotel Utah, Salt Lake City, Sept. 9-12. Mr. Harold Bowman, 42 S. Fifth East St., Salt Lake City 2, Executive Secretary.

Vermont State Medical Society, Mt. Washington Hotel, Bretton Woods, N. H., Sept. 20-22. Mr. Getty Page, 128 Merchants Row, Rutland, Vt., Executive Secretary.

Washington State Medical Association, Davenport Hotel, Spokane, Sept. 14-17. Mr. Ralph W. Neill, 1309 7th Ave., Seattle, Executive Secretary.

October

Academy of Psychosomatic Medicine, Park Sheraton Hotel, New York, Oct. 9-11. For information write Dr. Bertram B. Moss, Suite 1035, 55 E. Washington St., Chicago 2.

American Academy of Ophthalmology and Otolaryngology, Palmer House, Chicago, Oct. 12-17. Dr. W. L. Benedict, 100 First Avenue Bldg., Rochester, Minn., Secretary.

American Academy of Pediatrics, Palmer House, Chicago, Oct. 20-23. Dr. E. H. Christopherson, 1801 Hinman Ave., Evanston, Ill., Executive Secretary.

American Association of Medical Clinics, Palace Hotel, San Francisco, Oct. 2-4. Dr. John R. Hand, 1216 Southwest Yamhill St., Portland, Ore., Secretary.

American Association of Medical Record Librarians, Statler Hotel, Boston, Oct. 13-16. Miss Doris Gleason, 510 N. Dearborn St., Chicago 10, Executive Director.

American Association of Public Health Physicians, St. Louis, Oct. 27-31. Dr. Joseph M. Bistowish, P. O. Box 1117, Tallahassee, Fla., Secretary.

American Association for the Surgery of Trauma, Drake Hotel, Chicago, Oct. 2-4. Dr. William T. Fitts, Jr., 3400 Spruce St., Philadelphia 4, Secretary.

American Clinical and Climatological Association, Otesaga Hotel, Cooperstown, N. Y., Oct. 9-11. Dr. Marshall N. Fulton, 124 Waterman St., Providence 6, R. I., Secretary.

American College of Gastroenterology, Jung Hotel, New Orleans, Oct. 19-25. Mr. Daniel Weiss, 33 W. 60th St., New York 23, Executive Secretary.

American College of Surgeons, Conrad Hilton, Chicago, Oct. 6-10 Dr. Michael L. Mason, 40 E. Erie St., Chicago, Secretary.

American Dietetic Association, Bellevue-Stratford Hotel, Philadelphia, Oct. 21-24. Miss Ruth M. Yakel, 620 N. Michigan Ave, Chicago 11, Executive Secretary.

American Heart Association, Fairmont Hotel, San Francisco, Oct. 24-28 Mr. John D. Brundage, 44 E. 23d St., New York 10, Secretary.

American Otorhinologic Society for Plastic Surgery, Conrad Hilton Hotel, Chicago, Oct. 12. Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

American Public Health Association, Kiel Auditorium, St. Louis, Oct 27-31. Dr. Berwyn F. Mattison, 1790 Broadway, New York 19, Secretary

American School Health Association, St. Louis, Oct. 26-31. Dr. A O DeWeese, 515 E. Main St., Kent, Ohio, Secretary.

American Society of Anesthesiologists, Penn-Sheraton Hotel, Pittsburgh, Oct. 19-24. Dr. J. Earl Remlinger, 802 Ashland Ave., Wilmette, Ill., Secretary.

American Society of Plastic and Reconstructive Surgery, Drake Hotel, Chicago, Oct. 12-17. Dr. Kenneth L. Pickrell, Duke Univ. Hosp., Durham, N. C., Secretary.

American Society for the Study of Arteriosclerosis, Hotel Whitcomb, San Francisco, Oct. 24-26. Dr. O. J. Pollak, P. O. Box 228, Dover, Del., Secretary.

Association of American Medical Colleges, Ocean House, Swampscott, Mass., Oct. 13-15. Dr. Richard H. Young, 303 E. Chicago Ave, Chicago, Secretary.

Association of Life Insurance Medical Directors of America, Statler Hotel, Hartford, Conn, Oct. 22-24. Dr. Royal S. Schaaf, P. O Box 594 Newark 1, N. J., Secretary.

Association of Medical Illustrators, Dallas, Tex., Oct, Miss Rose M Reynolds, 42d & Dewey Ave., Omaha 5, Secretary.

Association of State & Territorial Health Officers, Hotel Washington, Washington, D. C., Oct. 22-24. Dr. Mack I. Stanholtz, State Office Bldg., Richmond, Va, Secretary.

Central Association of Obstetricians and Gynecologists, Hotel Leamington, Minneapolis, Oct. 2-4. Dr. Edwin J. DeCosta, 104 S. Michigan Ave., Chicago 3, Secretary.

Central Neuropsychiatric Association, Deshler Hilton Hotel, Columbus, O., Oct. 17-18. Dr. Ralph M. Patterson, Ohio State Univ., College of Med., Columbus 10, O., Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Oct 31-Nov. 1. Dr. Austin S. Weisberger, 2065 Adelbert Rd, Cleveland 6, Secretary.

Clinical Orthopaedic Society, Brown Palace Hotel, Denver, Oct 2-4 Dr. Charles H. Franz, 1801 Wealthy St. S. E., Grand Rapids, Mich., Secretary.

Congress of Neurological Surgeons, St. Francis Hotel, San Francisco Oct. 29-Nov. 1. Dr. Richard L. DeSaussure, 899 Madison Ave, Memphis, Tenn., Secretary.

Eastern Psychiatric Research Association, Inc., Brooklyn State Hosp., Brooklyn, N. Y., Oct. 23-24. For information write: Dr. David J Impastato, 40 Fifth Ave., New York.

Gulf Coast Clinical Society, Pensacola, Fla., Oct. 23-24. Dr J J Baehr, Jr., 117 N. Palafox St., Pensacola, Fla., Secretary.

Indiana State Medical Association, Murat Temple, Indianapolis, Oct. 13-15. Mr. James A. Waggener, 23 E. Ohio St., Indianapolis 4, Executive Secretary.

Pennsylvania, Medical Society of the State of, Bellevue-Stratford, Philadelphia, Oct. 12-17. Mr Lester H. Perry, 230 State St, Harrisburg, Executive Director.

Medical Society of Virginia, Hotel Jefferson, Richmond, Oct 12-15 Mr. Robert I. Howard, 1105 W. Franklin St., Richmond 20, Executive Secretary.

Mississippi Valley Conference on Tuberculosis, Biltmore Hotel, Dayton, Ohio, Oct. 15-18. Mrs. Augustus K. Maxwell, 1412 W. Washington Blvd., Chicago 7, Secretary.

National Proctologic Association, Hamilton Hotel, Chicago, Oct. Dr. George E. Mueller, 59 E. Madison St., Chicago 2, Secretary.

Oklahoma City Clinical Society, Biltmore Hotel, Oklahoma City, Okla., Oct. 27-29. Mrs. Alma O'Donnell, 503 Medical Arts Bldg, Oklahoma City, Okla., Executive Secretary.

Southwestern Medical Association, Pioneer Hotel, Tucson, Ariz, Oct 23-25. Dr. Russell L. Deter, 1501 Arizona St., El Paso, Tex., Secretary.

Western Industrial Medical Association, San Francisco, Oct., Dr. A C. Remington, 9851 Sepulveda Blvd., Los Angeles 45, Secretary.

Western Orthopedic Association, Multnomah Hotel, Portland, Ore., Oct. 22-25. Dr. Eldon G. Chuinard, 1922 N. W. Johnson, Portland 9, Ore., Secretary.

November

American Association of Blood Banks, Netherlands Plaza Hotel, Cincinnati, Nov. 20-22. Dr. John B. Alsever, 1211 W. Washington, Phoenix, Ariz., Secretary.

American College of Cardiology, Interim Meeting, Jung Hotel, New Orleans, La., Nov. 20-22. Dr. Philip Reichert, Empire State Bldg., New York 1, Secretary.

American Dental Association, Memorial Auditorium, Dallas, Tex., Nov. 10-13. Dr. Harold Hillenbrand, 222 E. Superior St., Chicago 11, General Secretary.

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THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 17 CHICAGO, ILLINOIS AUGUST 23, 1958

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CLINICAL MANAGEMENT OF IDIOPATHIC HIRSUTISM (ADRENAL VIRILISM)

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and
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Forty-five women with hirsutism were compared with 16 normal women as to various clinical features and laboratory findings, particularly the 24-hour urinary output of 11-desoxy, 11-oxygenated, and total neutral 17-ketosteroids. In seven of the patients the hirsutism was part of a surgically verified Stein-Leventhal syndrome; in 22 it was associated with irregularities of menstruation. There were also 16 patients in whom the hirsutism, generally less severe than in the others, coexisted with regular menstrual rhythm. Prednisone, in daily doses of 7.5 to 15 mg., reduced total neutral 17-ketosteroid excretion to normal in all patients and gave fair to good improvement as to hirsutism in all patients treated with it. Amenorrhea, oligomenorrhea, and menometrorrhagia responded remarkably to prednisone. The clinical results were gratifying. Physiologically they strengthen the belief that in hirsutism of this type the ovarian changes are secondary to primary changes in the adrenals.

IN A PREVIOUS communication,[1] 24-hour levels of urinary total neutral 17-ketosteroids, as well as those of the fractions $C_{19}O_2$ (11-desoxy derivatives, strong androgens) and $C_{19}O_3$ (11-oxygenated metabolites, weak androgens), before and after prednisone therapy, were reported in a small group of women with hirsutism. Total neutral and $C_{19}O_3$ 17-ketosteroids, although generally higher than in normal controls, were not consistently elevated. $C_{19}O_2$ fractions were always above normal, an observation of interest, since the $C_{19}O_3$ fraction contains metabolic end-products of weakly androgenic substances (11-β-hydroxyandrosterone, 11-ketoandrosterone, 11-β-hydroxyetiocholanolone, and 11-ketoetiocholanolone) and the $C_{19}O_2$ 17-ketosteroids include metabolites of strongly androgenic precursors (androsterone, etiocholanolone, and dehydroepiandrosterone). Prednisone, in appropriate doses, lowered $C_{19}O_2$ fractions to or almost to normal levels and also reduced or eliminated excess hair growth. We have now had considerably more experience with this problem and would like to report a method of clinical management.

Method

This report includes 45 women with hirsutism and 16 normal controls. After a complete history was taken and physical examination was done, the

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Clinical and laboratory data in 16 patients with hirsutism and regular menstrual rhythm are shown in table 4. Hirsutism was generally less than in preceding groups. The levels of total neutral 17-ketosteroids were above 15 mg. in only 4 women (mean, 13.3 mg.), and those of the $C_{19}O_2$ fraction were above 6.0 mg. in 9 of 14 subjects (mean, 6.5 mg.). The low level in the patient in case 52 likely was due to laboratory error, since only 25% of the total enzyme value was recovered. Levels of $C_{19}O_3$ were above normal in seven and within the normal range in seven women (mean, 5.5 mg.). The patient in case 47 showed some regrowth of facial hair with cessation of prednisone therapy; the patient in case 52 developed acne with doses above 5 mg. per day. We cannot determine the incidence of hair regrowth as yet, but 17-ketosteroids and fractions remained normal a minimum of 12 months in some patients. Acne was troublesome in three instances with doses of over 5 mg. per day, when original $C_{19}O_2$ levels were normal.

Data are available in a few patients with hirsutism associated with other conditions. One of us (W. H. P.)[6] reported hirsutism of typical distribution in children with hypothyroidism, which disappeared after six to eight months of thyroid therapy; two untreated children were studied. A 9-year-old girl showed total neutral levels of 5.7 mg., with that of $C_{19}O_2$ 1.3 mg. and that of $C_{19}O_3$ 2.4 mg.; a 9-year-old boy had similar values of 4.3, 1.5, and 2.7 mg. respectively. No control values for children of similar age are available, but these levels appear to be normal, suggesting an extra-adrenal etiology. Similarly, a 4-year-old girl with hypertelorism and extensive generalized hirsutism excreted 2.1 mg. of total 17-ketosteroids, 0.6 mg. of $C_{19}O_2$, and 2.6 mg. of $C_{19}O_3$.

Two women undergoing menopause, with facial hirsutism since onset of amenorrhea, showed total levels of 11.1 and 13.3 mg., $C_{19}O_2$ values of 3.3 and 5.8 mg., and $C_{19}O_3$ levels of 5.2 and 8.5 mg. Hair growth involved the chin and upper lip, with little, if any, elsewhere. Normal $C_{19}O_2$ levels in these patients suggest an extra-adrenal etiology. Two female pseudohermaphrodites, with surgically proved adrenocortical hyperplasia, were studied. One, 5 years old, showed total levels of 29.2, a $C_{19}O_2$ level of 12.8, and a $C_{19}O_3$ level of 13.9 mg. Ten mg. of prednisone per day for 30 days depressed the total level to 24.0 and that of $C_{19}O_2$ to 3.0 mg. but raised that of $C_{19}O_3$ to 19.5 mg. Reduction in the level of the $C_{19}O_2$ fraction is understandable on the basis of adrenocortical suppression, but the rise of that of the $C_{19}O_3$ moiety is difficult to explain. The other, aged 7 years, who incidentally showed gross and microscopic Stein-Leventhal changes in the ovaries, had no fraction levels determined prior to treatment, but total levels were as high as 24.5 mg. After treatment with 7.5 mg. of prednisone per day the total level fell to 10.5 and that of the $C_{19}O_2$ and $C_{19}O_3$ fractions fell to 3.0 and 3.5 mg, respectively.

TABLE 3.—*Urinary Levels of 17-Ketosteroids, in Milligrams of Androsterone per Twenty-four Hours, in Twenty-two Patients with Hirsutism and Abnormal Menstrual Function*

	Before Therapy						17-Ketosteroids Level During Therapy				Final Results	
		17-Ketosteroids Level										
			Fractions					Fractions				
Case	Hirsutism, Grade	Total Neutral	$C_{19}O_2$	$C_{19}O_3$	Prednisone, Mg./Day	Days of Therapy	Total Neutral	$C_{19}O_2$	$C_{19}O_3$	Total Days of Therapy	Hirsutism	Menses
24	4	20.2	8.0	8.1	0							
25	4	18.5	8.4	4.2	0							
26*	3	21.6	10.5	5.9	10.0	42	5.4	3.8	3.6	234	Good	Improved
27	3	8.4	...	...	10.0	46	6.5	2.6	3.1	203	Good	Improved
28	3	13.2	5.2	5.4	0							
29*	3	28.2	16.8	7.2	10	183	6.8	...	...	265	Good	Improved
30*	3	17.0	...	...	10	67	6.3	2.6	3.5	420	Good	Improved
31*	3	25.7	14.6	6.9	10	28	12.3	5.6	6.0	370	Good	Improved
32*	3	22.2	...	...	10	89	8.5	5.7	3.2	388	Fair	Improved
33*	3	17.8	11.5	5.7	10	35	5.9	2.2	3.3	268	Good	Improved
34*	3	22.4	13.2	6.6	10	41	5.7	3.7	2.4	302	Fair	Improved
35	3	18.1	...	...	7.5	219	7.0	...	...	357	Fair	Improved
36*	2	37.8	17.5	14.8	7.5	175	5.2	2.9	3.1	250	Good	Improved
37*	2	15.1	7.1	3.9	10.0	26	5.9	5.2	1.8	236	Good	Improved
38	2	8.2	5.8	3.9	0							
39*	2	14.5	6.5	4.0	15.0	19	4.1	3.7	2.2	406	Good	Improved
40*	2	22.7	...	...	0	85	12.7	7.5	7.6	633	Good	Unchanged
41*	2	10.3	2.8	7.0	0							
42	2	18.4	6.1	4.2	0							
43	2	10.5	3.5	2.7	0							
44*	2	9.1	7.0	1.9	0							
45*	1	8.8	6.2	6.9	2.5		—	—	—	120	...	Improved
	Mean	17.8	8.9	5.8			7.1	4.1	3.6			
	Range	8.2-37.8	2.8-17.5	1.9-14.8			4.1-12.7	2.2-7.5	1.8-7.6			

*Clinical impression, Stein-Leventhal syndrome.

Comment

The ratio of $C_{19}O_2$ to $C_{19}O_3$ 17-ketosteroids varied markedly within the normal group, but mean values were almost identical. No normal control excreted over 6.1 mg. of $C_{19}O_2$, and all of seven

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THE PROBLEM OF THYROID NODULE IN AN ENDEMIC GOITER AREA

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The incidence of cancer in nodular goiters removed at Sacred Heart Hospital, Spokane, was 7%. In 60% the cancer was considered benign clinically and even at the time of surgery. Nodules of any type in patients under 30 years of age have proved malignant in 37% of cases. Of the nontoxic multinodular goiters, 5.7% were malignant in this series. The incidence of cancer appeared to be much higher in those with a history of recent growth or pressure symptoms or with firm discrete nodules. These signs and symptoms seem to be definite indications for surgical investigation. It is felt that all nodules in young people should be treated surgically.

The concept of surgical management for nodular goiters has recently been challenged,[1] and proper management of the patient with a nodular goiter now presents a problem to many conscientious physicians. In the absence of toxicity, substernal extension, pressure symptoms, or cosmetic deformity, is surgery really indicated, or can one ignore the goiter or treat it medically without fear of malignancy? Unfortunately, if one turns to the current literature, a mild state of confusion is frequently only compounded. Statements that 5-10% of goiters are malignant and that all should be removed[2] are countered by claims that the incidence of cancer in goiters is probably in the range of 0.5%.[3]

Incidence and Diagnostic Data

Incidence.—The following survey was undertaken simply to seek out some useful conclusions which might help with the management of the numerous such patients seen in Spokane, a goitrogenic community. In this study, the records at Sacred Heart Hospital, one of three large institutions serving this area, have been utilized. During the three-year period of 1953 to 1955 inclusive, 32 patients were discharged with a diagnosis of cancer of the thyroid gland. Nine of them subsequently developed metastasis, and four died during the period of this study, indicating that this is not a benign disease. Twenty patients lived in Spokane County, the population of which was estimated to be about 250,000, giving an annual incidence of 3.5 per 100,000. This is slightly above the incidence recently estimated for the San Francisco Bay area,[4] and, since these figures are derived from the

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Read before the annual meeting of the Spokane Surgical Society, Spokane, Wash., April 12, 1958.

records of only one of three large hospitals in Spokane, the incidence of thyroid cancer must be at least as great, if not greater, in this goitrogenic community.

Time and Nature of Diagnosis.—Of the 32 patients, three had had previous surgery and entered the hospital for palliative treatment only. One patient died in cardiac failure, and at autopsy a completely unsuspected carcinoma of the thyroid with cervical node and visceral metastasis was found to be the cause of death. The record of another patient was so incomplete that it could not be utilized except for numerical inclusion. Thus, only 27 cases were discovered at operation.

During this same period, 438 thyroid operations were done at this institution with no operative mortality. Of this number, 50 were performed for toxic diffuse goiter and 7 for nontoxic diffuse goiter. Carcinoma was found in none of these glands, and, since this survey is directed at nodular goiters, these patients are not considered. This leaves 381 cases of nodular goiter in this series. Twenty-seven cancers in 381 patients gives an over-all incidence of 7% for malignancy.

The diagnosis of cancer was clinically obvious in 4 of these 27 cases. That is, the patient had a stony-hard thyroid mass and palpable cervical lymph node metastasis. In seven cases malignancy was suspected because of such factors as firm, solitary tumors, rapid growth, and local fixation. In 16 cases the diagnosis was not suspected clinically, or at least no mention was made of the fact on the patient's record. Of even more importance, at the time of operation, when the surgeon could see and feel and actually hold the tumor in his hands, it was considered benign in 17 of the 27 malignant cases. In five of these, frozen section was done immediately and the diagnosis established in three. The remaining 12 cases were considered so typically benign that frozen section studies were not even requested. If an experienced surgeon holding a resected tumor in his hands cannot recognize carcinoma, it seems obvious that a diagnosis of a benign nodule on the basis of its physical characteristics on clinical examination is totally unreliable. Thus, a search has been made for other factors which might assist in selecting suspicious cases for surgical therapy. Clinical suspicion of carcinoma does carry definite weight. Of 22 cases in which the surgeon recorded his suspicion, malignancy was found in 11 (50%).

Age and Sex Distribution.—Malignancy was found in 13 (4%) of the 324 patients between 30 and 69 years of age, in 5 (28%) of those over 70, and in 14 (37%) of those between 10 and 29 years of age. In this latter group, incidentally, the lesions varied in consistency from stony hard to soft and cystic.

Sex in this study was not a significant factor. Sixteen per cent of the nodular goiters were in men, yet they comprised only 6% of the cancer group, a surprisingly low figure. This is certainly at variance with most recorded series, in which the relative incidence of cancer is consistently higher in males.[5]

Duration of Nodules.—Concerning the duration of nodules, in the malignant group the goiter was present less than one year or found on routine examination in 60%, existed one to five years in 15%, and was present for over five years in 25%. In the benign group the corresponding figures are 52, 27, and 20% respectively. Duration appears to be of no value in pointing out suspected goiters, but it is interesting that 25% of patients with malignant goiters complained of thyroid nodules of five years' duration or longer, a factor confirmed by numerous investigators.[6]

Types of Goiter

There were 180 nontoxic nodules believed to be solitary on physical examination. Seventeen, or just under 10%, of these proved to be malignant. Incidentally, 77 of these patients were found to have multiple nodules at the time of surgical exploration, and six of the nodules were cancerous. Thus, of nodules proved to be truly solitary at the time of surgery, 12% were malignant, and even when the clinical impression was disproved and multiple nodules found the incidence of cancer was only slightly less than 10% is this series. I feel that this confirms the seriousness of discrete nodules. Ten of these cancers were unsuspected, or, to express it in different terms, about 7% of solitary nodules which clinically seemed benign were actually malignant. One hundred twenty-three patients were operated on for nontoxic multinodular goiter, and 5.7% of these had cancer. Four (about 3%) were not suspected. Of the toxic goiters, 70 were multinodular. Three cancers, all unsuspected, were found in this group, an incidence of about 4%. None of the eight solitary toxic nodules was cancerous.

Forty-six per cent of the patients with nontoxic multinodular goiters complained of either recent growth or pressure symptoms, whereas this was a complaint in only 18% of those with toxic goiter. Since the latter are frequently actively secreting hyperplastic glands, it is not unusual that nearly 20% of patients with this type did complain of recent growth. On the other hand, it is a surprising finding in 50% of patients with nontoxic goiter and indicates that these represent a select group on the part of referring physicians and not the general run of patients with differentiated adenoma (thyroid) seen in everyday practice. A high proportion of these goiters had firm, discrete nodules; this also indicates selection. And, as a matter of fact, except for the group under 30 years of age, most of the patients with cancer in multinodular glands had either very firm, discrete nodularity or a history of recent growth.

It has been stated by some that cancer and nodular goiter are two completely unrelated conditions, that is, that cancer arises as frequently in an otherwise normal gland as in a goitrous gland. As proof, they cite the high incidence of solitary cancerous nodules where the remaining gland presents no abnormality. Although I have seen no reports in the literature on this subject, the high incidence of patients in this series who had additional surgery for breast nodularity or fibroid uterus might add weight to the argument that hormone imbalance is involved in nodular goiters. Also, the high rate of recurrent goiters, 18 cases (about 4%), is significant. Perhaps there is an element of hormone deficiency, and many of these patients might benefit from prolonged courses of therapy with supplementary thyroid extract after removal of the nodules.[7] Certainly there is room here for further investigation.

On the other hand, if one accepts hormone deficiency as the sole factor in goitrogenesis, why do 25% of the patients with known cancer have a history of goiter of five years' duration or longer, and why do many cancers originate in preexisting adenomas? It is also difficult to understand why the incidence of carcinoma in diffuse goiters should be in the range of 0.5 per cent,[5a] and yet in multinodular goiters it is consistently reported as above 5%, as in this series. As was mentioned above, some workers claim that this is due to selection,[8] that is, that only suspected cases are referred for surgery.

The fact that 50% of the patients reported here with multinodular goiter presented with complaints of recent growth or pressure symptoms does force one to concede that this objection may have some merit. However, the patients operated on for toxic nodular goiter were, in all probability, operated on primarily for toxicity—fear of malignancy being an afterthought—and yet 4% did show malignancy. I suspect that this may be a closer figure to the actual incidence of malignancy in multinodular goiter in this community rather than the figure of 5.7%.

As was mentioned above, there was no operative mortality in this entire series, and in the 381 cases complications were recorded in 14 (about 3%). Most of these were minor, such as mild transient hypoparothyroidism (4), wound bleeding and hematoma (3), postoperative hemorrhage (2), superficial phlebitis (1), transient hypocalcemia (1), and fever of unknown etiology for several days (1). In one instance the patient complained of hoarseness for several weeks, but her voice then returned to normal. The only complication of a serious nature was one instance of cardiac arrest during the induction of anesthesia. This responded to fist percussion of the chest wall; the surgeon then proceeded with the operation, and recovery was uneventful. These figures indicate the procedure of thyroidectomy carries a minimal risk in this community.

Summary and Conclusions

The incidence of cancer in nodular goiters removed at Sacred Heart Hospital, Spokane, is 7%. In 60% the cancer was considered benign clinically and even at the time of surgery. Whereas a clinical impression of benign nodule means nothing, a clinical impression of malignancy carries considerable weight; 50% of cases so diagnosed proved malignant. Nodules of any type in patients under 30 years of age have proved malignant in 37% of cases. It is felt that all nodules in young people should be treated surgically. Sudden growth of a goiter in patients over 70 years of age was caused by cancer in over 25%, and it would seem these should be also treated surgically. In addition, surgical excision of all solitary nodules is recommended, since about 10% are cancerous. Although not borne out in this series, the incidence of cancer in males with goiter must be regarded seriously, in view of the consistency of the literature on the subject.

Of the nontoxic multinodular goiters, 5.7% were malignant in this series. The incidence of cancer appeared to be much higher in those with a history of recent growth or pressure symptoms or with firm discrete nodules. These signs and symptoms seem to be definite indications for surgical investigation.

In my opinion, the 5-to-10% figure for malignancy frequently quoted for multinodular goiter is very probably due to selection. On the other hand, the 0.5% incidence quoted at the opposite swing of the pendulum is too low, at least in this community, where 3 to 4% of stationary goiters contain unsuspected cancer. The decision for or against surgery in these patients is a difficult one, and probably should rest on one's own teaching, philosophy, and convictions and possibly those of the patient in some instances. Those who decide on a conservative course must be aware and assume the responsibility that in 3 to 4% of these cases unrecognized cancer possibly is present.

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THE BIRTH AND DEATH OF SPECIALTIES

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> I am convinced that the conception of specialism dominant to-day is a wrong one, and that helpful as this specialism has been in many ways, nevertheless, instead of enlightening, it tends to darken understanding in a cloud of detail. That each new phenomenon discovered by methods simple or recondite, is of importance in adding to our knowledge of disease, is accepted as a truism, and on that ground specialism seems justified. But there are other matters in the recognition of a phenomenon beyond its discovery which are essential to the progress of medicine.
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> Sir James Mackenzie, in Future of Medicine, London, H. Frowde, 1919.

It is interesting that, while much has been written on the rise of specialties, no one, to the best of my knowledge, has noted the fact that specialties also die. Nor has much study been given to the generic phenomenon of specialism in medicine, that is, to the varieties of determining forces which engender specialism in medicine. There are a number of competent histories, each of which treats of the origin and development of an individual specialty. But there is no history of specialism as such.[1]

That confronts us with an intriguing problem. For surely it must have struck many a thoughtful person that the phenomenon of specialization, not merely in terms of the specialties developed but as a dynamic experience within medicine itself, merits study and exposition. How is it then that there are so many individual histories of individual specialties but no analytic or dynamic history of specialism?

While this is an intriguing problem, the answer in effect is quite simple. Most medical historians identify the history of specialism with the history of modern medicine. Arturo Castiglioni,[2] for example, dates the origins of specialism from the 17th century. "Thus," he writes, "at the end of this [the 17th] century, when the cooperation of medicine and the natural sciences was being emphasized, we already see outlines of the essential features of the great structure of experimental science. Already various specialties began to be detached from the main trunk. . . . Here we have an extensive preparation for modern medicine." Castiglioni's vision of modern medicine as a continuous and accelerated detachment of various specialties from the main trunk of medical practice is shared almost universally; indeed medical history seems to support and validate this vision. And yet, persuasive as this vision may appear to be, there crowd on one's mind a number of troubling awarenesses and a host of questions that somehow cannot be reconciled with it. There comes to mind, for example, the history of surgery. In the days of Hippocrates, the physician was a surgeon as well as a clinician, and he was no less esteemed in the one role than he was in the other. Some among the followers of Æsculapius were notably skilled in setting broken bones, in lancing festering sores, and in dressing the wounds caused by sword and spear, and they were properly noted for their skills. But they were physicians first and surgeons incidentally.

The common factor in medical specialism can only be described in negative terms. A specialist is one who does not practice comprehensive medicine. He exercises his skills only in some subdivision or in some partial function within the larger framework of medicine. The summation of the practices of the specialties does not, in effect, constitute the practice of comprehensive medicine. As a science, ecology is the study and exposition of the multiple, and often of the subtle, effects, which both living and nonliving entities exercise one on another, and the many among themselves. As far as man is concerned, ecology is a humbling and a leveling science. It reveals that in the embracing scheme of things, in the scales of ecologic nature, man weighs no more ponderously than does the vibrio of cholera, the spirochete of syphilis, or the bacillus of phthisis. Man is the only one of nature's creatures who has learned how to manipulate ecologic nature. Diseases have been conquered not by the clinical or surgical specialties but by ecologic and physiological medicine. The future of medical service is not to be envisaged as a continued refinement, as well as increase, in the specialties, with the consequent parceling out of the patient to a host of men, who will care for him and treat his illnesses. Rather, within two generations, medicine as a science, and medical care, will undergo a revolutionary change brought about not by the economic, legislative, or social manipulations of well-meaning men but by the maturation of those knowledges and intelligences embraced in physiological, and in ecologic, medicine.

Sixth Herman L. Reiss Memorial Lecture, read before the New York Academy of Medicine, Oct. 28, 1957.

> History has preserved for us some information about practitioners called surgeons; but between the separation of surgery (and also operative surgery), to the profit of a few individuals, while all parts of the art of healing were studied and practiced by most doctors, and a real division of medicine into three branches practiced by three classes of practitioners, there is an immense distance on which it is not necessary to dwell further. These surgeons are precisely the men who were pushed by a special bent or by necessity toward one part of the art of healing rather than another. Furthermore we see that these practitioners can be most often placed in the class of specialists, properly speaking, a class that was no less numerous in antiquity than in modern times, as we learned from Galen (Utrum med. sit, an gymn. hyg. ch. 24, vol. 5, pp. 846 ff., and De partib. artis medicae, ch. 2, vol. 4 [in Spuriis libris], f° 16, ed. Junt.). If Galen is forced to admit the existence of specialties, he rises up against specialists, insofar as these half or quarter physicians, as he says, wished to consider their specialties as distinct parts of medicine, which is one, whatever its divisions may be. Thus this very separation of surgery and the extension given to this word prove decisively that the division into three branches was purely scientific and had no exact status in practice.[7]

The Hippocratic books on surgery (On Wounds and Ulcers. On Hemorrhoids, On Fistulae, On Injuries of the Head, On Fractures, On Reductions of Dislocation) were addressed to the very same practitioner who found instruction in the Aphorisms and who was taught to see the ecologic relations of man in "On Airs, Waters, and Places." Surgery was a phase of medicine, even as were diet and pharmacology.

It is reported that the Romans did not hold the physician in high esteem. Cato is said to have warned the Romans against both Greek literature and Greek medicine. "When the Greeks have flooded us with their literature and especially their physicians, they will ruin everything for us" is a statement credited to him. And yet the immortal Galen, who was Greek by birth, was famed and esteemed as a physician in imperial Rome.

Insofar as the Romans did prize the physician they favored him alike as surgeon and as clinician. With the decline of Rome and the advent of what is so picturesquely, but erroneously, termed the Dark Ages, surgery somehow became separated from medicine, and thereafter its practitioners were looked upon as a "scurvy lot." Physicians then were no longer surgeons, and surgeons were not physicians. They were, in the main, barbers or butchers by trade, or otherwise itinerant "handymen." Yet the Middle Ages were not without some truly famed surgeons; there were Guido Lanfranchi [d. 1315], Henri de Mondeville [1260-1320], and Guy de Chauliac [1300-1367], to name but three. It is noteworthy that these men who did so much to advance surgery are as one in lamenting the decline of the practice of surgery by physicians. "Physicians regarded it as undignified to practice surgery, and especially blood letting, but left them both in the hands of barbers," complained Bruno de Longoburgo in his Chirurgia Magna.

At this point we may properly ask "what happened to bring surgery, once so highly esteemed in the practice of medicine, down to so low a level?" Again, and to anticipate our further treatment of the subject, we may ask "what was it that subsequently redeemed surgery and made of it not only an honored, but, as I am told, a highly rewarding practice?" Surgery, it should be noted, was rehabilitated long before the advent of modern medicine, that is, before bacteriology, asepsis, and anesthesia. Of John Hunter (1728-1793) it was said that "he found surgery a mere mechanical art, and, left it a beautiful science," and also that he "made gentlemen out of surgeons." The latter statement, if taken literally, is a dubious compliment, but the observation is intended to be taken historically rather than literally. I raise these questions with no intention to pursue them. My purpose in citing the history of surgery was merely to point out that the vision of the development of medicine as a process whereby the specialties detach themselves from the main trunk to flourish anon just is not correct. It does not conform to reality.

The Lay Origin of Specialism

Nor for that matter is this vision supported by the history of other specialties. It may not prove flattering to the "professional origins" of the orthopedist, the dentist, the oculist, the proctologist, the urologist, and the dermatologist, to name but a few, but it is true that the practitioners in each of these specialties from the Middle Ages down to recent times were in the main minstrels, mountebanks, and quacks, that is, sharpers of every kind and variety. I am not sure we are entirely fair to these stalwart pioneers, for sharp they surely were, and they had to be; no doubt among them there were also many men of high skill, fine dexterity, and of much practical, if not of academic, wisdom. Be that as it may, the lithotomist, the bone setter, the lens coucher, the fistula mender, and the extractionist were specialists who plied their specialties long before medicine itself had become diversified.

We must conclude then that specialization is therefore not concomitant with, nor is in itself, a gauge of the advancement of medicine. Historically, medicine was never more specialized than as it was practiced in ancient Egypt. In "The Persian Wars" (volume 2, page 84), Herodotus reported that in Egypt "Each physician applies himself to one disease only, and not more. All places abound in physicians; some physicians are for the eyes, others for the head, others for the teeth, others for the intestines, and others for internal disorders."

From this we may conclude that in the history of medicine specialism is a problem apart. It is not, as some have affirmed, and many believe, the inevitable concomitant and the logical resultant of scientific progress. (Indeed, the long view of the history of science reveals the pattern of periodic diversifications in interest and knowledge, that is, of specialization, followed by periods wherein the synthetic unification of knowledge is achieved. Science is never more innately consonant and rewarding than during its unitary stages.)

But if specialism is a problem apart, then what indeed is it? Before treating of it further, we require precise definitions of specialism, specialties, and specialists. For on examination we find that the term and the concept of a specialty and of a specialist relates to a number of diverse professional functions. There are specialists in single diseases as, for example, the tuberculosis specialist, or the syphilologist. There are specialists in the use of singular instrumentalities, as, for example, the x-ray specialist. There are operational specialists, as, for example, the surgeons and the obstetricians. There are specialists in single organs, as the eye specialist, and of single systems, as the neurologist or the gynecologist. It is true that none of these specialties is insular and that the specialists who pursue them have an overlapping knowledge of other departments of medicine. Yet the significant conclusion that can be drawn from the most ample catalogue of the different references which the terms specialty and specialist carry amounts to this: the common factor in medical specialism can only be described in negative terms. A specialist is one who does not practice comprehensive medicine. He only exercises his skills in some subdivision or in some partial function within the larger framework of medicine.

Specialism and Comprehensive Medicine

This definition is not intended to be, nor is it, basically derogatory. It is purely descriptive. It is also historically most suggestive and most significant. Allow me to project certain of its telling implications. One is that with the advancement of medicine comprehensive medicine as such cannot, and is not, to be practiced. Only the specialties are liable to be practiced. The other telling implication is that the summation of the practices of the specialties in effect constitutes the practice of comprehensive medicine, that is, of total medicine. Here we encounter the reversal of the famous dictum that the whole is greater than the sum of its parts. Specialism implies that "the sum of the parts is equal to the whole." Group practice does not publicly subscribe to these convictions, but they are inherent in the rationale and procedures of group practice, which, in effect, amounts to the deliberate structuring of "basic specialists" in a close cluster pattern.

Specialism in medicine, however, long antedated group practice. Group practice is merely the latter-day logical development of the theoretical concepts on which modern medicine is founded. These theoretical concepts can best be described as specificism in the etiology of disease and in therapy. The concern of modern medicine was deliberately and avowedly fixed on disease. The specific causes of specific diseases, the specific treatment of specific diseases, and the specific prevention of specific diseases comprise the three principal branches of modern medicine. The pursuit of these concerns is best effected by specialization. Hence our specialists and specialties, all of which, with the possible and partial exceptions of pediatrics and obstetrics, are concerned and occupied with disease.

Modern medicine has not been concerned with health, save only in the negative sense of "the seeming absence of disease." It has been almost entirely occupied with the "conquest of disease." It has openly subscribed to the faith that health is to be gained only in the conquest of disease. Von Behring formulated, professed, and proclaimed this faith. It has not been disavowed, at least not by an appreciable number of medical leaders, though some few, the late John Ryle for one, have protested and have argued that the seeming absence of disease cannot be equated to health, nor is health to be gained in the "serial" conquest of disease.

The concept embraced in the conquest of disease is seemingly very simple. In effect, however, it is enormously complicated and, incidentally, of dubious validity. In its simple and popular form, popular among physicians no less than among the informed laity, it corresponds to Ehrlich's analogy of the magic bullet. Modern medicine, it is postulated, discovers the malignant agent which causes disease, then contrives a magic bullet, which, like the guided missile of the military, finds its mark, the malignant agent, and destroys it. Then there is no more disease, and by that token, the person who was ill is now well. He is healthy.

The interesting thing is that medicine can boast of few specifics, that is, of few magic bullets, and even those deemed to be specifics do not function quite like guided missiles. It is also very questionable whether medicine has conquered any appreciable number of diseases. We may claim that much for medicine only if we embrace under the term medicine all the biological sciences, including the sciences of hygiene and sanitation. But that is a loose, and to my mind not only unwarranted but confusing, extension of the range of medicine. I would limit the meaning of "medicine" to that which is practiced by the physician in relation to his patient. It is after all here that we find the specialism with which we are concerned.

Physiological Versus Clinical Medicine

In this purview it can be seen that the physiologists have contributed more to the conquest of disease than have the clinicians, that is the medical practitioners, specialists included. Furthermore and perforce the physiologists have been more deeply concerned with the normal than with pathology. Their contributions have obviated disease by pointing the ways to the maintenance and fostering of health. The physiologists have not been specificists, for health is not a specific factor but the resultant of many contributing, correlated factors (witness Claude Bernard's magnificent concept of homeostasis).

I cannot undertake to support this affirmation with many data, nor do I think it necessary that I do so. Yet I would refer to the contributions which the science of nutrition, primarily and essentially a physiological discipline, has made to the conquest of disease, chiefly in enabling us knowingly to promote well-being. One needs but think of the conquest of rickets, with its multiform complications ranging from long-bone deformity and pelvic distortion to tetany, to gain some idea of the protean beneficial effects of this science. Endocrinology is another physiological discipline with far-reaching effects in the conquest of disease. It is worth noting that there is more than a casual relationship between nutrition and endocrine function, as may be witnessed, for example, in the role of iodine in thyroid function. Indeed it is not all a bizarre assumption that what are classed as trace elements among the chemical components of the body may play a very determining role in the functions of the endocrine system. Our growing knowledge of the operations in the human economy of the trace elements, I am certain, will not only enable us to promote well-being but may contribute phenomenally to the conquest of disease.

On a par with the physiologists in their telling contributions to the conquest of disease stand the public health scientists. Yet their functions, their operations in the field of health promotion and disease control and prevention, are difficult to define. That is so, in part, because their operations are so varied and so numerous and also because, perforce, some phases of public health have been tinged with specificist theories and ideas. Public health has, like medicine, suffered from an excessive preoccupation with disease. That, however, has been so only during the past 150 years. During its long history, which extends over more than 2,000 years, public health has been, in essence, the science of man's ecology. Public health, from the most ancient times on, has served and guided man in the effective manipulation of his environment. This science above all others has enabled man so greatly to increase in numbers and to spread to the four corners of the earth.

Medicine and Human Ecology

The Hippocratic classic "On Airs, Waters, and Places" was a primer in human ecology. I emphasize human, for it lies in the nature of man even merely to desire salubrious environments but even more to render those places where he lives fitting to his wants and needs. Man is a manipulator and, in a measure, the master of his environment. Animals go to the water hole, but man sinks wells, builds aqueducts, and in various other ways fetches water to serve his needs—precisely where his needs are. Man, to reiterate, does not helplessly yield to his environment: he manipulates it, he bends it to his will in a thousand ways and more. Of course, the extent to which man can manipulate his environment with safety, and to his enduring advantages, has its limits. That, incidentally, is a realization not yet fully or widely appreciated. Impressed with the many things man can do and has done with and to his physical environment, many are unmindful of the collateral effects and labor in the persuasion that man can do anything and everything—in time. In this man is an ecologic ignoramus.

That public health is essentially the science of human ecology is not a common persuasion. I expect it will become so in time. For basically it is a sound and an illuminating identification. Considered in this light the main enterprise of public health, as well as its major achievements, become intelligible as a consistent performance. Otherwise they seem but a miscellany of separate acts, to be catalogued in such categories as water supervision, sewage and garbage disposal, food inspection, and nuisance control. Even so seemingly singular an achievement as the production of an effective vaccine against poliomyelitis, when examined in its larger and deeper relations, can be recognized as an achievement in ecologic control and adaptation. Commonly it is viewed as a "miracle" in viral immunology. In its lesser dimensions, it is all of that, but in effect it is an ecologic adaptation of great significance.

Since this is a point of significance in the larger argument which we are pursuing, I must develop it in more ample dimensions and in finer detail. Ecology is not a term that can be defined with facility, for it refers not to a thing nor to many things but rather to relations, that is, to relations between things and to the relation of relations between things, the things being of many orders and varieties. As a science, ecology is the study and exposition of the multiple, and often of the subtle, effects, which both living and nonliving entities exercise one on another, and the many among themselves.

As far as man is concerned, ecology is a humbling and a leveling science. It reveals that in the embracing scheme of things, in the scales of ecologic nature, man weighs no more ponderously than does the vibrio of cholera, the spirochete of syphilis, or the bacillus of phthisis. Contrary to the illusions bred by the evolutionism of the 19th century, man is not Nature's darling, nor is he Creation's favorite. Ecologic nature has no favorites and manifestly does not fend for man against the rest of its creatures. Ecologic nature is seemingly committed to but one objective, to the maintenance of what might be termed a cosmic homeostasis, that is, not to allow, or better still, to disenable one from among its many kinds of creatures to gain an unbalancing dominance over the rest. When the hawks outbreed the mice and rats, they evoke the ecologic countereffect of starvation—till balance is once again established between hawks and rodents.

That ecologic nature is not always effective in maintaining cosmic homeostasis, in the rather crude sense, is evident by the historic emergence of certain new species and the disappearance of certain old ones. Man's achieved preponderance, numerically and power-wise, in the living world, likewise witnesses the fact that ecologic nature is manipulable. But this is only so under given conditions.

Man is the only one of nature's creatures who has learned how to deliberately manipulate ecologic nature. He is not, however, always mindful of the fact that she is only manipulable but never to be corrupted or traduced save with dire consequences. Under any circumstances there is always a premium to be paid, a tribute to be rendered to ecologic nature for every novelty that is introduced into the established order.

Man runs into the menace, or into the brunt, of disaster whenever he forgets this exaction of an ecologic *quid pro quo*. It is not possible, as was attempted during the Industrial Revolution, to herd great masses of humans into filthy slums, to work them long and hard, to feed them miserably on an inadequate diet, without suffering the retribution of plagues and of untimely deaths. It is not possible, as we are beginning to perceive, to disrupt the traditional and long-established patterns of the familial interrelations of husband and wife, and of parents and children, without encountering the untoward and manifold effects of social delinquency, adult no less than juvenile. The point, of course, is not that we should have avoided the Industrial Revolution with its emergent urbanism, nor is it that we should seek to retain the family pattern of, say, the Victorian Era. That is not the point at all. It is rather that we need be mindful of the broad ecologic changes effected by the immediate alterations in the patterns of our existence and seek to compensate for them. That is what public health has endeavored to achieve, whenever public health has been at its best. It is an ecologic compensation to fortify bread with the very elements initially extracted from the grain during the milling process, when the process is an ecologic requisite to the feeding of urban populations dependent for their daily bread on commercial, mass bakers. It is an ecologic manipulation to expose an individual by means of vaccines or other antigens to a controlled encounter with noxious agents in order to achieve deliberately what ecologic nature might accomplish indifferently, to wit, the basis for a coexistence between "germ and man" favorable to the inoculated individual.

Public Health as an Ecologic Discipline

Ecology as a science and public health as the science of human ecology are subjects too vast and too complicated for ample treatment as subtopics. They are major subjects by virtue of their innate significance and dimensions. I have brought them into my exposition in order to identify them, together with physiological medicine, as the two disciplines which, far more than clinical medicine, have contributed to the "conquest" of disease and to the advancement of well-being, that is of health. And, as I am sure you must by this time anticipate, it is my conviction that the future in medicine belongs to these two, to ecologic medicine and to physiological medicine, the last dealing with the normal and optimal internal milieu of the individual, and the first, that is, ecologic medicine, with man's external milieu, in its broadest and deepest implications.

Yet what of the specialties? Seemingly we have wandered far from our committed theme. In truth, however, I've not forgotten my commitment. The long excursion was to my mind necessary, for as you will recall, I have argued that the specialties were developed chiefly as a result of modern medicine's predominant concern with disease. Then, as we have seen, diseases have been conquered not by the clinical or surgical specialties but by ecologic and physiological medicine. The conquest of certain diseases has effected the death of certain specialties. In this dictum both "conquest" and "death" must be understood in a relative rather than in an absolute sense.

I have referred to a number of diseases once common and now rare. Among them are rickets, chlorosis, and cretinism. To these we may add a number of other diseases not perhaps entirely rare but certainly of markedly diminished prevalence and of lowered demographic significance. Tuberculosis is one, and an ecologic disease par excellence. Syphilis and gonorrhea assuredly have been conquered in the effective if not in the absolute sense. What then has happened to the venereal disease specialist and to his specialty? The surgery necessitated by the sequelae of the Neisserian infections, in both male and female, but especially in the female, has greatly been reduced. Reflect on what has happened to the surgical otologist whose *raison d'être* were the chronic ear infections and the mastoid involvements? The dermatologist, one of the earliest among the specialists, has perhaps proportionately lost more terrain than any other specialist. Consider, for example, that broad class of skin disorders, formerly falling within the realm of the dermatologist, which have literally evanesced under the impact of the physiological illuminations of nutrition and of endocrinology.

With all this in mind I submit that what has happened during the past quarter of a century is more than likely to be extended and intensified during the coming decades. I mean that we have witnessed only the infancy of physiological medicine and that the full import of ecologic medicine remains yet to be grasped, even by those in the vanguard of medical progress. Many more specialties will be revolutionized in the not too remote future.

The Promise of Physiological Medicine

It is not at all playing the vainglorious role of the prophet to prognosticate the proximate resolution of a substantial number of the mysteries that surround certain among the leading causes of death—specifically of malignant growths, atherosclerosis, coronary disease, and malignant hypertension. To this list I might add, just to come closer to home, the diseases of dental decay. Nor is it too wild a guess that much of the illumination that will dissipate the mysteries surrounding these diseases will come by way of physiological explorations into the normal. To envisage the effects of these much to be hoped for developments, think what a blessing to mankind, and how ruinous for dentists it would be, were it really possible to prevent dental caries. I do believe this possibility will eventuate. I do not, however, think it will be ruinous for dentists. They will simply work less hard and more effectively in other directions. Similarly, think how much of surgery will be obviated when we have learned to control the neoplastic growths; this, too, is within realistic prospects.

The combined research attack, now being focused on atherosclerosis and coronary disease, notably along the tangents of the metabolic fate of fats, promises, I am confident, some fundamental insight into the physiological derivation of these disorders. Since metabolism is under the sway of the endocrine system, it is not rash to anticipate the uncovering of some implicated endocrinologic fault in the atherosclerotic processes. Nor should we overlook the apparently significant role of exercise in the retardation of these disorders, as has been so clearly demonstrated in the epidemiologic studies of J. N. Morris.

On the future of cancer research I dare not venture a prognostication, save in the most general terms, namely that cancer, or better the neoplasms, will yield their mystery to physiological research centered on the complexities of embryologic growth, reparative tissue growths, and the mechanisms of their provocation and arrest. Here the morbid and malignant lie too close to the "life creative and normal" not to be under the sway of similar if not identical principles.

This portion of my presentation, however, fills me with uneasiness, and I must hasten to get beyond it. Indeed, I must disavow any seeming pretense to the gifts of prophecy. For such a gift I lack the requisite knowledge and the sublime faith in self that is even more requisite than knowledge. It was not my intention to say precisely how these major diseases will be eliminated but rather that they will be in the foreseeable future, most probably because of our growth in physiological knowledge and by the cultivation of better ecologic medicine. When that happens, we will witness the "death" of other specialties currently preeminent.

The Future of Medical Service

What I mean to convey is this: the future of medical service is not to be envisaged as a continued refinement, as well as increase, in the specialties, with the consequent parceling out of the patient to a host of men, who will care for him and treat his illnesses. I think rather that within two generations, that is before the second millennial year is reached, medicine as a science, and medical service perforce, will have undergone a revolutionary change, in many respects as profound as that effected by the rise of bacteriological sciences. This revolution will not be brought about by the economic, legislative, or social manipulations of well-meaning men but by the maturation of those knowledges and intelligences embraced in physiological, and in ecologic, medicine. Unless global disaster puts an end to civilization and to science, the eventuations I have sketched are to my mind inevitable.

I am conscious of the fact that in my presentation I have been somewhat light in my treatment of present-day medicine, including its specialists. I may have thus given you an erroneous idea of the esteem in which I hold contemporary medical science and its practitioners. I deem them both of the highest order. Were I grievously sick and had I the choice to be sick in any age in history, from the time of Hippocrates to the present, I would choose none but the present. For at no time in the history of man has the practitioner of the healing art been as tutored in the skills and as well armed with as great a multitude of means to fend against the ravages of sickness, and even more against pain and suffering, as he is today.

But as I have argued and as is clear to all thinking men, the treatment of disease is not the equivalent of the promotion of health and well-being—and specialists treat disease.

I am not so sanguine in my hopes for mankind, nor so naïve, as to believe that man will ever so manage his life as to have no need for "cures" and for the specialist who ministers them. I can envisage an attrition in specialties and specialists but not their total elimination from the medical scene or corps. It is only that I can see the future of medicine as lying in directions other than greater and ever greater specialism.

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ABSENCE OF ACTIVE IMMUNIZATION AGAINST INFECTIOUS HEPATITIS

FOLLOW-UP STUDY AFTER ADMINISTRATION OF GAMMA GLOBULIN

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Recipients of either gamma globulin or gelatin, during the field studies of 1951 and 1952 for the evaluation of gamma globulin as a prophylactic agent against poliomyelitis, were studied to observe the effect of the same gamma globulin against infectious hepatitis. The total number of reported cases of hepatitis and the cumulative rate in each area during the five-year period after injection were as follows. Of a population of 10,794 who received gamma globulin, there were 20 cases of hepatitis (1.9 per 1,000); of 10,794 who received gelatin, there were 16 cases (1.5 per 1,000); and of 14,155 not given injections, there were 46 cases (3.2 per 1,000), for a total of 82 cases from a population of 35,743 (2.3 per 1,000). It seems certain that these lots of gamma globulin did not contain an inactive or attenuated agent capable of producing an active immunity against clinical hepatitis and that gamma globulin did not produce hepatitis in these areas.

Gamma globulin has been established as an effective prophylactic agent against infectious hepatitis.[1] The dose required for prophylaxis has been comparatively small and has ranged from 0.01 to 0.06 ml. per pound of body weight in various studies. Administration of gamma globulin has at times been followed by unexpectedly long periods of protection against clinically apparent hepatitis.[2] Since protection has persisted for several months, even with doses in the lower range of effectiveness, some factor in addition to the passive transfer of antibody must be operative. This seems particularly true in view of the fact that the half-life of homologous gamma globulin (labeled with radioiodine [I^{131}]) in man is three weeks or less.[3] This short half-life is consistent with prior observations of protection against measles and poliomyelitis, since protection appears to wane within three to eight weeks.

Stokes[4] recently reviewed the possible mechanisms involved in prolonged immunity against hepatitis after administration of gamma globulin. Of the mechanisms suggested, the most probable appeared to be that of active but clinically inapparent infection occurring relatively soon after the administration of gamma globulin and resulting in a long-lasting "passive-active" type of immunization. Attempts to reproduce this mechanism experimentally have not as yet yielded conclusive results.[5]

Another possible mechanism for the persistent immunity observed may be the presence of small quantities of either attenuated or inactivated hepatitis agent in the gamma globulin. This agent, while apparently not producing illness, might stimulate active immunity of a degree sufficient to prevent subsequent disease. Since large pools of plasma have been shown to contain hepatitis-producing agents comparatively frequently[6] and since various viruses have been incompletely cleared from gamma globulin when plasma is fractionated by current commercial methods,[7] this mechanism for immunity appears to be a possibility requiring further attention.

Materials and Methods

The persons studied were recipients of either gamma globulin or gelatin during the field studies of 1951 and 1952 for the evaluation of gamma globulin as a prophylactic agent against poliomyelitis.[8] These field studies involved the inoculation by random selection of children of specified ages with either gamma globulin or 1.5% gelatin-solution placebo in doses averaging 0.14 ml. per pound of body weight. Only two of the three original areas were suitable for this review, since records of individual cases of hepatitis were not available from the third area. The first area studied was Utah County, Utah, where 5,720 children of ages 2 to 8 years were inoculated, half with gamma globulin and half with gelatin, in 1951. A total of 6,800 children of similar ages were estimated to be in the "observed control" group in this area. The second geographical area was Woodbury County, Iowa, and adjacent Dakota County, Nebraska, with an inoculated child population of 15,868 and observed noninjected controls estimated to number 7,355. The ages included in the latter area were 1 to 11 years, and all inoculations were given in 1952. At no time was the type of material injected disclosed to the participants.

All cases of hepatitis reported to the local health departments[9] during the five-year period after inoculation were analyzed for participation in the inoculated group of the study, and, if study par-

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ticipants (verified by name, address, and date of birth), they were analyzed by type of inoculum received. Cases of patients with similar names but with discrepancies regarding either date of birth or address were verified prior to inclusion in the inoculated group.

A total of 73 cases of hepatitis were reported during the 10 years prior to the date of injection in Utah County.[9b] The maximum number of cases in any one year was 27 and the median number was 4. Cases had been reported in 8 of these 10 years. In Woodbury County the situation was quite different. Only five cases were reported during this 10-year period, and all of these cases were reported in a single year. It must be pointed out that reporting of hepatitis was not required or requested until about the time of the institution of the field studies.

In regard to other factors concerned with completeness of reporting in the case of hepatitis, it should be pointed out that gamma globulin for the prophylaxis of hepatitis among household contacts was provided by the health department in Woodbury County beginning in 1949.[9a] Gamma globulin had similarly been issued in Utah since about 1950.[9b] Consequently, one can expect that reporting of this disease would be considerably more complete after these dates, since reporting is necessary to acquire the prophylactic material.

Cases of Hepatitis Reported from Two Study Areas Among Recipients of Gamma Globulin and Gelatin and Among Noninjected Children of Similar Ages

Year of Report	Utah County				Woodbury-Dakota County				Totals			
	Injected Group				Injected Group				Injected Group			
	Gamma Globulin	Gelatin	Not Injected*	All Cases†	Gamma Globulin	Gelatin	Not Injected*	All Cases†	Gamma Globulin	Gelatin	Not Injected*	All Cases†
1950	...	...	...	0	...	...	...	0	...	...	0	0
1951‡	0	0	0	3	...	...	...	16	0	0	0	19
1952§	0	0	0	1	...	...	...	32	0	0	0	33
1953	0	0	2	4	0	0	0	0	0	0	2	4
1954	0	0	1	1	6	7	12	50	6	7	13	51
1955	2	1	7	17	8	3	13	46	10	4	20	63
1956	0	1	0	3	4	2	7	28	4	3	7	31
1957	...	...	...	...	0	2	4	17	0	2	4	17
Totals	2	2	10	29	18	14	36	189	20	16	46	218

* Same age as injected, but not inoculated during the 1951 Utah County study or 1952 Woodbury-Dakota Study. Probably includes new residents, as well as those present, but not injected, at the time of the study.

† All cases reported from area, regardless of age or injection status.

‡ Injections given in Utah County.

§ Injections given in Woodbury and Dakota Counties. All 1952 cases prior to injections.

Results

A total of 218 cases of hepatitis were reported from the two study areas during the five-year period after the establishment of the injection clinics. Eighty-two of these hepatitis cases were reported in children whose age indicated they would have been eligible for injection at the time of the field trials. On checking the records of injection, we found that 36 of these children had received either gamma globulin or gelatin in the 1951 or 1952 clinics. The table indicates all cases of hepatitis reported by age group, by year of onset, and by injection status. Inspection of this table suggests that hepatitis, although present in both areas prior to clinics, was not prevalent in either of the study groups or the noninjected contacts for more than a year after the injection period. The sudden complete absence of this disease for 18 months in Iowa, after 32 cases had been recorded earlier in 1952, is interesting but extremely difficult to evaluate. When cases began to appear again in these areas they occurred in the two injected groups with approximately equal frequency. The slight excess of four cases in the total gamma globulin group is probably not significant and represents an excess of cases in one area three years after injection.

The total number of cases of hepatitis and the cumulative rate in each area during the five-year period after injection is as follows. Of a population of 10,794 who received gamma globulin, there were 20 cases of hepatitis (1.9 per thousand); of 10,794 who received gelatin, there were 16 cases (1.5 per thousand); and of 14,155 not given injections, there were 46 cases (3.2 per thousand), for a total of 82 cases from a population of 35,743 (2.3 per thousand).

This summary suggests that the rate, as expected from the numbers in the table, is slightly higher in the group of patients who had received gamma globulin than in the gelatin group. This difference is not believed to be of significance. The considerably higher rate in the "observed controls" may be somewhat misleading. Although there have been no additions to the population in the gamma globulin and gelatin groups, and indeed probably some attrition of these groups has occurred due to population mobility, the "observed controls" group contains all new arrivals to this area as well as those present in this population at the time of inoculation. In addition to this problem two additional factors also enter. It must be remembered, first, that the uninoculated is an estimated population and hence may be subject to some error and, second, that the gamma globulin and gelatin groups were selected from persons who volunteered to take these substances, a factor that may vary with socioeconomic factors. Since it is apparent that hepatitis also may be correlated with socioeconomic status, valid comparison between injected and "observed control" groups, particularly over this long period, is not possible.

A large follow-up study of the possible presence of serum hepatitis virus in gamma globulin was made in 1951, at the time of the pilot study on gamma globulin and poliomyelitis in Utah County, Utah.[8] Twenty weeks after the four-day clinic period 5,767 questionnaire post cards were mailed to the parents of the inoculated children requesting information regarding the incidence of eight specified infectious diseases during the intervening period. The main purpose was to obtain information regarding hepatitis, but questions were also asked about influenza, mumps, chickenpox, scarlet fever, measles, rubella, and pertussis. Inquiry regarding hepatitis was asked for under the term "jaundice" or "yellow jaundice." Common names were also used for all other diseases. An unexpectedly good response was obtained in that 5,244 cards were returned, representing 91% of those mailed. The results are as follows: 2,652 persons received gamma globulin; one person who received gamma globulin and one who received gelatin had hepatitis; 626 who received gamma globulin and 610 who received gelatin had influenza; 113 who received gamma globulin and 133 who received gelatin had mumps; 118 who received gamma globulin and 100 who received gelatin had chicken pox; 11 who received gamma globulin and 10 who received gelatin had scarlet fever; 14 who received gamma globulin and 6 who received gelatin had measles; one who received gamma globulin and 5 who received gelatin had rubella; none who received gamma globulin and 4 who received gelatin had pertussis.

Measles and rubella are the only diseases with unexpected differences of possible significance. The majority of these cases occurred more than 10 weeks after the injections, so no effect from the inoculation would be expected. It is probable that there was a confusion in diagnosis between the two types of measles, accounting for the apparent differences between those given gamma globulin and those given gelatin. The one case of jaundice after administration of gamma globulin occurred in an 8-year-old female only three weeks after the injection. It was an asymptomatic jaundice of one week's duration, seen only once by a physician. He made no diagnosis except jaundice. This incubation period is too short for serum hepatitis. Two other siblings of this patient, aged 4 and 7 years, did not become ill, nor did the parents.

Comment

Although the reporting of hepatitis in these areas may not be complete, there is no reason to expect differences in reporting between recipients of either gamma globulin or gelatin. Changes in the size of these two groups due to population mobility should not alter the relative proportions at risk. Therefore, the conclusion seems inescapable that nothing was present in these lots of gamma globulin that might provide a long-lasting active type of immunization. Unfortunately, insufficient numbers of cases of hepatitis occurred in these areas during the period immediately after inoculation to permit any estimate of the duration of the effect of large doses of gamma globulin on the incidence of hepatitis. It seemed certain, however, that the duration of this effect, even with these relatively enormous doses, is less than two years and is probably considerably less than this.

The data regarding absence of clinical jaundice during the 20-week period covered by the post card survey appear to offer convincing evidence of the absence of active hepatitis virus in gamma globulin given in relatively large doses in the largest series (2,652 children) followed to date.

Summary

The reported incidence of hepatitis over a five-year period in 10,794 recipients of gamma globulin and 10,794 individuals who did not receive gamma globulin and who were of similar distribution regarding age, sex, weight, and geographical area has been determined. There is no evidence of significant differences in the frequency of hepatitis in either group during the five-year period. It was not possible to determine the duration of the passive prophylactic effect, since insufficient cases occurred in these areas during the first two years of the period studied. It seems certain from these data that these lots of gamma globulin did not contain an inactive or attenuated agent capable of producing an active immunity against clinical hepatitis. Post card survey data regarding 2,652 children offered convincing evidence that active hepatitis agent is not present in gamma globulin as prepared by current commercial methods of plasma fractionation.

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This study was aided by a grant from the National Foundation for Infantile Paralysis.

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CLINICAL NOTES

TREATMENT OF TAPEWORM INFESTATION

REPORT ON AN EFFECTIVE TREATMENT WITHOUT TOXIC EFFECTS ON HOST

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The beef tapeworm (Taenia saginata) and the pork tapeworm (T. solium) are the two most common forms of taeniae found in the Boston area. We have had no experience with the use of the method described in this report in the treatment of the fish tapeworm (Diphyllobothrium latum) or of the dwarf tapeworm (Hymenolepis nana) Man is the primary host for all of these parasites, and in all but the dwarf tapeworm one or more intermediate hosts are necessary for the full life cycle to take place.[1] The adult taeniae live in the small intestine of man, their heads attached to the mucosa of the duodenum or jejunum.[2] They have no digestive tracts but absorb food through their body walls. The body of the worm, which may be as long as 15 ft., is made up of numerous segments each of which discharges ova from an oviduct When the eggs are eaten by a suitable host (the cow for T. saginata and the pig for T. solium), they hatch in the intestine and the larvae migrate by they become encysted. When the infested meat in the raw or insufficiently cooked state is eaten by man, the cysts are liberated in the digestive tract way of the bloodstream into the muscles, where and the tapeworm head enclosed in the cyst becomes attached to the intestinal wall and grows into an adult worm in one to three months. The habitation in the intestine usually causes no symptoms. The patient seeks medical help when he observes the proglottides in the stool as gray, flat, squirming, ribbon-like structures.

On rare occasions the patient may reinfect himself and become the intermediate as well as the primary host. This occurs when the ova are regurgitated or are transmitted to the mouth; the active larvae liberated in the upper digestive tract invade the bloodstream and become encysted in the muscles. This condition, which is known as cysticercosis, may cause severe symptoms, including fever, muscle pains, and central nervous system irritation with convulsions [1]

Many different drugs and chemicals have been used in the extirpation of tapeworms, the rationale being to give a drug that is toxic for the head of the worm so that it will relax its hold on the mucosa long enough to permit expulsion of the entire worm by strong catharsis. It is well known that, even when the long segmented body of the worm is expelled, if the head or scolex does not come away the worm will regenerate. The extract of male fern (aspidium oleoresin) has been used for many years but has never been fully satisfactory because of its frequent inefficacy, the disagreeable taste, and the occasional severe, and sometimes serious, toxic side-effects on the patient.[3] The table lists some other drugs that are used and indicates their reported efficacy. All of these drugs which have toxic effects on the worm are also toxic for the host.[4]

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In recent years many reports attest to the good to excellent results obtained with quinacrine (Atabrine).[5] Nausea and vomiting still occur in many patients, but sodium bicarbonate administered with the quinacrine is said to prevent this. Other reports indicate successful treatment when the transduodenal tube was utilized to administer quinacrine as well as oleoresin, hexylresorcinol, carbon tetrachloride, or tetrachloroethylene.[6] It should be remembered that all of these drugs are potentially harmful. Quinacrine, of course, has not been reported as lethal, although occasionally it has caused severe, prolonged retching.

In 1932, De Rivas[7] presented a study which demonstrated that T. solium and T. saginata could not survive for more than five minutes if immersed in either glycerin or saline solution warmed to 130-140 F. His study reported excellent results in curing tapeworm-infested patients when these solutions were administered through a transduodenal tube. Our report concerns the results obtained with this method of treatment.

Results Reported in Literature of Treatment of Patients with Tapeworm Infestation

Drugs Employed	Patients Treated, No.	Cures, No.	Failures, No.
Aspidium oleoresin by transduodenal tube[4a]	87	62	25
Carbon tetrachloride[4a]	16	12	4
Tetrachloroethylene[4b]	8	3	5
Hexylresorcinol[4b]	24	7	17
Tin (Cestodin)[4c]	202	180*	22
Quinacrine (Atabrine)[4d]	488	347	141

* No scolices recovered.

Materials and Method

This study is based on the data obtained from the histories of 40 patients hospitalized during the years 1930 to 1958. In all of these cases, the diagnosis was based on demonstration of proglottides, ova, or both. The same therapeutic procedure was carried out in all cases. Before the treatment is begun, the following articles should be ready at the bedside: (1) a Rehfuss tube, (2) a 50-cc. syringe, (3) a bottle of glycerin, (4) a bottle of saturated magnesium sulfate solution, (5) a thermometer (preferably centigrade), and (6) 500 cc. of sterile saline solution.

The procedure for treatment is as follows. 1. Pass a Rehfuss tube into the stomach. 2. Turn the patient on his right side and allow the tube to pass into the duodenum. 3. Check the tube by fluoroscope to be certain that the tip is well down in the second or third portion of the duodenum, beyond the ampulla of Vater. 4. When certain the tube is in position, introduce 1½ oz. of magnesium sulfate solution through the tube. 5. Then introduce immediately 1½ oz. of glycerin. 6. Then introduce immediately 2 oz. of a mixture of equal parts of magnesium sulfate and glycerin. 7. Then introduce immediately 500 cc. of the sterile saline solution which has been warmed to a temperature of 54-60 C or 130-140 F. A bucket and a bedpan should be ready in the patient's room. The bucket should contain warm water or saline solution so that if the worm is obtained it can be preserved and identified.

Results

No untoward reaction other than a flushing sensation has been noted. Two patients had mild tachycardia. In the great majority of cases the entire worm, with scolex attached, was expelled within 10 to 15 minutes after the treatment had been completed. Of the 40 patients treated, 31 immediately obtained successful results, and in these the scolex was identified. In five other cases the scolex was not demonstrable. Follow-up studies of one to five years in these five patients failed to reveal evidence of continued infection, and they are regarded as cured. Of the remaining four patients, two did not respond to any degree and did not pass any segments. The last two patients were unable to tolerate intubation, and, although they are not classified as treatment failures, they are representative of failure of the method and thus are included in our study. In summary, 36 of 40 patients treated by intubation (as described above) were cured of the tapeworm infestation.

Comment

It should be emphasized that no toxic drugs are required in the procedure outlined. Furthermore, the opportunity to demonstrate the worm and the scolex within a few minutes of completion of treatment is a point of great satisfaction to both the physician and the patient. It is true that the method requires the time of a physician or someone adept at passing a duodenal tube and also fluoroscopic facilities for positioning the tube in the duodenum. We have carried out all of the procedures in a hospital, but conceivably, if the required facilities are available, it could be done in the office. As far as the patient is concerned, the treatment does not make hospital care necessary either before or afterward.

Intubation may be objectionable to some; however, the delight of the patient in seeing the worm almost immediately on termination of the procedure is ample reward for the discomfort entailed in swallowing the tube. It does not seem likely that this method would be as applicable to young children. The youngest patient treated by us was 12 years of age.

Summary

Patients with tapeworm infestation have been successfully treated by transduodenal intubation. For this method, toxic drugs are not required. Glycerin, magnesium sulfate, and saline solution warmed to 130 F were introduced through the tube. Thirty-six of 40 patients were cured. Two were unable to tolerate intubation.

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NEGATIVE REAGIN TESTS IN MARITAL PARTNER OF PATIENT WITH SECONDARY SYPHILIS

THIRD INDICATION FOR TREPONEMA PALLIDUM IMMOBILIZATION TEST

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In a previous issue of THE JOURNAL[1] we said that heretofore there were two indications for the treponema pallidum immobilization (TPI) test but that to these should be added a third. We recommended this test in the following situations: (1) to help distinguish between the biologically false-positive and true-positive blood test for syphilis; (2) to assist in establishing a diagnosis of syphilis in patients who have clinical evidence of the disease, particularly in late syphilis, but who have negative blood and spinal fluid serologic tests; and (3) to assist in the diagnosis of syphilis in a patient with epidemiologic evidence of the disease but with negative clinical and serologic findings.

As illustrative of the third indication, a case was presented wherein an 8-year-old boy, examined by us in 1955 because of a positive reaction to the Hinton test, proved on clinical examination to have congenital syphilis. However, his mother repeatedly had negative clinical and serologic (reagin) findings. The diagnosis of syphilis in the mother was established by the TPI test, thereby confirming the clinical diagnosis of congenital syphilis in the offspring. The present case is another and more common example of a patient who has epidemiologic evidence of syphilis but with negative clinical and serologic data.

Report of a Case

A 27-year-old woman was admitted to the outpatient department on Oct. 23, 1957, because of generalized arthralgia, headaches, sore throat, and fatigue, even after a good night's sleep, for the past three months. In addition, she complained of blurring of vision for the past month or so. Her symptoms were not related to any acute disease and were gradual in onset. She weighed 112 lb. (50.8 kg.), which was 8 lb. (3.6 kg.) under her usual weight. The Hinton blood test was positive. Except for her complaint, the system history was negative and so was the physical examination. There was a family history of tuberculosis, a maternal aunt having died of this disease, but periodic x-ray examination of the chest had been negative.

The social history was more revealing. The patient had been married for seven years and had two children, a girl aged 6 and a boy aged 4. Her husband was two years older than she, and they had enjoyed a happy married life up to

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about five years previously, when he was in the service. When he returned from overseas he began to drink heavily and go out with other women. Although his wife was pregnant at that time, he abused her and was arrested on three occasions for beating her up. Although he was physically and verbally abusive to her, he had never failed to support her financially. On his discharge from the Army in 1954, the abuse continued and she prepared to get a separation. He promised to reform, and thereafter he did not physically abuse her, but he continued to make unsavory remarks. He showed no interest or affection for the children. After the birth of her child in 1953, she had avoided marital relations whenever possible.

A Hinton blood test done on Oct. 23 was positive. The patient returned to the outpatient department a week later, still complaining of generalized arthralgia, headache, sore throat, and fatigue. Six days previously a generalized maculopapular rash had developed. It was discrete, painless, nonpruritic, and infiltrative and involved the face, trunk, and upper extremities and less so the thighs and legs. There were discrete split papules on the palms and others on the soles. There were no mucous patches or condylomas. The patient's last exposure was three weeks previously with her husband. She denied any other exposures.

A diagnosis of secondary syphilis was made, and treatment was begun immediately. That evening she had a typical Jarisch-Herxheimer reaction, characterized by chills, fever, severe bone and muscle pain, intensification of the sore throat and headache, and enlargement and reddening of the skin lesions. She completed the course of treatment without any difficulty.

The patient was asked to bring her husband and two children in for an examination. The two children were clinically and serologically negative. The husband denied any history of syphilis or other venereal disease, but on a subsequent visit he admitted having contracted gonorrhea while in the Army, for which he had received treatment. He denied extramarital exposures except for the time he spent in the service. He admitted drinking heavily but had never lost a day's work because of it. Two months previously he had been admitted to a hospital because of a chemical burn on the genitals, caused by the spilling of kerosene on his clothes while he was at work. Swelling and edema of the penis developed, with phimosis necessitating a dorsal slit.

The physical examination at the clinic was negative. Quantitative Hinton tests on Nov. 2, 9, and 14 were also negative. A Hinton test on Nov. 23 was doubtful. On Nov. 14 a lumbar puncture was performed; the spinal fluid contained two cells; the total protein was 35 mg. per 100 cc.; the gold sol curve was 0011100000; and the Davies-Hinton test was negative. However, TPI and Treponema pallidum complement fixation (TPCF) tests, also performed on this day, were positive, thereby establishing a diagnosis of syphilis in the husband. After repeated questioning the patient recalled that during his hospitalization in the previous summer he had received two daily injections of penicillin because of balanitis. A transcript of his hospital record confirmed this and that he was admitted to the hospital on Aug. 5. It also stated that four days after admission a qualitative Hinton test was positive, and in view of this report the genital lesions were reexamined. They did not appear to be either primary or secondary syphilitic eruptions but had the earmarks of a chemical burn. A repeat Hinton test was negative on Aug. 16.

This patient was evaluated, and a course of penicillin was given consisting of 6 million units. The treatment was started on Nov. 25; two days later the quantitative Hinton blood test was positive in whole blood, and it was again positive five days later. Treatment was completed on Dec. 6, but in spite of his wife's repeated urging he did not return to the clinic for post-treatment examination until April 12, four months later.

Epidemiologic Analysis

This 27-year-old housewife had completed her treatment on Nov. 10, 1957. Two months later the Hinton blood test was negative. Blood samples taken on Feb. 1, March 1, and April 12 remained negative. On each visit to the clinic the patient was interviewed concerning extramarital contacts. These she denied, and it is our belief that she was telling the truth. Her husband, on the other hand, when brought to the clinic by his wife, never asked such questions as why he was being examined, what was the matter with his wife, why we wanted to do a lumbar puncture, and why we took the repeat blood tests. He never volunteered any information and answered questions briefly and to the point. Although his visits to the clinic were in the morning, he always had a strong odor of alcohol on his breath. He denied extramarital relations since getting out of the Army but admitted to heavy drinking, though he did not drink to the point where he lost time from work. He admitted that he might have had extramarital relations with someone he met at a bar, but if he had he could not recall who she was and when the event occurred. Even though it was explained to him that whatever information he gave us would be privileged and that his wife would not know of any extramarital activities, the patient steadfastly maintained that he could not remember any extramarital relations. When asked how his wife picked up her disease, he replied, "She no doubt got it from me." He labeled as absurd any possibility of his wife cheating on him. "She's not that kind of a girl," he said. "She had plenty of chances when I was overseas; instead she preferred to stay with her mother and be loyal to me." How did the patient explain his disease? He must have picked it up when he was too drunk to remember. At the conclusion of treatment, he failed to return to the clinic for post-treatment examination until four months later. He then admitted to an extramarital exposure in July, 1957, naming the contact, who proved to be infected.

Summary and Conclusions

A married woman had the most infectious stage of syphilis, the secondary. Her husband on repeated examination had no clinical or laboratory evidence of this disease. Epidemiologically his chances of escaping infection, had he been the innocent partner, would be small indeed. However, the presence of the disease in him was established through the Treponema pallidum immobilization and Treponema pallidum complement fixation (TPI and TPCF) tests, which were positive.

It has been repeatedly stated that penicillin or any other antibiotic adequate for a particular disease the patient may have had, but inadequate for syphilis, may render reagin tests negative, thus making the diagnosis of syphilis at a later examination difficult and at times impossible to establish. The husband was treated for gonorrhea in the Army four years ago. The amount of penicillin given is not known. He again received penicillin intramuscularly, 300,000 units a day for two days, three months prior to his initial examination. We do not know how much penicillin or other antibiotic he may have received.

In the light of this experience, when a physician is confronted with infectious syphilis in one spouse, repeated examinations of the other spouse should be performed, and if these all are negative the contact should have the benefit of TPI and TPCF tests before being discharged as not infected. As a corollary, spouses of infected patients with latent or late syphilis who have negative clinical and reagin test examinations for syphilis should also have TPI and TPCF tests performed before discharge.

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OUTPATIENT TREATMENT OF POSTALCOHOLIC SYNDROME

RESPONSE OF TWO HUNDRED FORTY-THREE ALCOHOLICS TO PROMAZINE HYDROCHLORIDE GIVEN ORALLY

Harold I. Goldman, M.D., Denver

Many general hospitals lack the facilities to treat the withdrawal symptoms of acutely exacerbated chronic alcoholism. The postalcoholic syndrome thus must often be managed on an outpatient basis. It devolves on the private physician to determine and to apply the most effective treatment.

The aim of therapy is alleviation or prevention of the symptoms of the postalcoholic syndrome—ranging from severe headache and insomnia to nausea, vomiting, tremulousness, acute hallucinosis, and incontinence of bowels or urine. Past efforts to control the postalcoholic syndrome in outpatients have been generally unsuccessful.[1] Properly administered, several agents introduced in recent years can prove helpful in such outpatient treatment. Our experience has included fair success with both mephenesin[2] and mephenesin plus glutamic acid.[3] Reserpine and certain other ataraxics also have been evaluated by other investigators.[4] However, such drugs fall short of the ideal therapeutic agent.

A therapeutically efficacious agent obviously will prevent development of withdrawal symptoms or will control those already present. In addition, the drug selected should (1) mitigate the craving for alcohol prevalent in such patients, (2) act directly on the central nervous system, since most symptoms of the syndrome originate there, (3) produce a rapid response, (4) be relatively long-acting, orally effective, and diminish rather than aggravate gastrointestinal hypersensitivity, and (5) be safe for administration without close medical supervision.

Promazine (Sparine) hydrochloride is an ataraxic of proved value in the hospital treatment of alcoholism. It also appears to possess many of the properties of the ideal therapeutic agent for outpatient management of the postalcoholic syndrome. Fazekas and associates[5] have reported that promazine effectively controlled excitation, acute tremulousness, hallucinosis, and delirium tremens in a series of 263 hospitalized alcoholic patients and have commented favorably on the drug's antiemetic and sedative properties. Figurelli[6] found that promazine successfully controlled delirium tremens within 48 hours in the majority of 187 hospitalized alcoholics.

Conditions of Study and Medication

I have treated a small number of alcoholic patients in private practice with promazine, which successfully controls the postalcoholic syndrome present. The current series of 243 patients were public charges seen in my capacity as police surgeon. All patients were examined in the Denver city jail infirmary after their arrest for conspicuous drunkenness. All exhibited two or more of the symptoms that make up the postalcoholic syndrome. Hallucinosis and tremulousness were most commonly seen. Some form of antisocial behavior (usually aggressiveness) was noted in 170 patients.

The sole aim of therapy was control of the symptoms of the postalcoholic syndrome to assure that the patients might face an examining magistrate with minimum delay and with comprehension of the legal proceedings. No attempt was made to treat the underlying chronic alcoholism. Most outpatients were chronic alcoholics, both "repeaters" and "spree drinkers," with a long history of arrests on charges arising from their alcoholism. A number had associated debilitating diseases. The patients' ages ranged from 16 to 74 years, with the greatest number between 30 and 50 years.

Every effort was made to avoid the semblance of any treatment other than routine, in the eyes of the alcoholic patient. The physical examination each received on admission and the regular examinations performed thereafter formed a pattern established before the study began and was familiar to those alcoholics previously jailed. Blood pressure readings and other procedures ascertaining patient response to promazine caused no special interest and were accepted as normal by all. Patients with delirium tremens on arrest and those who developed delirium tremens after imprisonment were hospitalized immediately and excluded from this study.

Promazine hydrochloride, 100 mg. perorally, was administered under the supervision of the police surgeon immediately after imprisonment of the patients. The dose was repeated every four hours until all symptoms associated with the postalcoholic syndrome disappeared. In a few selected cases, an initial oral dose of 200 mg. was given. Therapy was generally continued for 12 hours, but in a few patients it was extended to 36 hours.

Response to Promazine Therapy in 243 Alcoholic Outpatients

		Improved*		Unimproved	
	No.	No.	%	No.	%
Male	133	124	93	9	7
Female	110	105	96	5	4
Total	243	229	94	14	6

* Complete remission of symptoms referable to postalcoholic syndrome.

Method of Evaluation and Results

Clinical appraisal of outpatients for purposes of such a study as this will always present problems. So only two categories were tabulated: improved and unimproved. Improved response was defined as complete remission of symptoms referable to the postalcoholic syndrome. A patient was classed as improved only if he was completely sober when facing the examining magistrate. If any vestige of the postalcoholic syndrome could be detected by the police surgeon, the patient was classed as unimproved.

Prior experience with alcoholics in the same prison environment as in the present study permits a general group-to-group comparison. Our own observation confirms that of other investigators; without treatment, the mild to severe symptoms of the postalcoholic syndrome can persist unimproved beyond 96 hours.

The table lists responses to promazine. No side-effects, toxic or allergic, were observed in any patient receiving 100 mg. of promazine, nor was hypotension noted. In a few cases where an initial dose of 200 mg. was given, mild hypotension developed; blood pressure in one patient dropped about 15 points to 100/80 mm. Hg; this patient was hospitalized as a precautionary measure and made an uneventful recovery. No other side-effects were encountered.

Comment

Reduction of aggressiveness was not a primary aim in this study. Yet it should be noted that promazine completely controlled aggressiveness or boisterousness. The first 100-mg. dose was observed to quiet even the more abusive or exuberant alcoholics. Emesis presented no problem in the study. No patient retched continuously, and if a tablet of promazine remained on the stomach as long as 10 minutes, the antiemetic properties of the drug apparently acted to control nausea, for no vomiting was noted beyond that time.

Cell blocks confining alcoholics are well known for their high noise levels, a mélange of alcoholic whoops, profane language, and loud chatter. The contrast following oral promazine medication is astonishing. If awake, patients most often exhibit the well-behaved demeanor seen in a physician's waiting room. Within 45 minutes after receiving the first dose of promazine, orally, the average alcoholic falls into a light sleep. Slumber, our experience has shown, usually indicates that control of the postalcoholic syndrome is to occur.

Where sleep does not follow the first 100-mg. dose, the patient should be carefully observed. Underlying emotional tension of considerable magnitude undoubtedly exists. Failure to respond to an initial 100-mg. dose of promazine, given orally, will most often coincide with the more severe abstinence symptoms in the postalcoholic syndrome. Our results suggest that patients who respond well to an initial dose of promazine recover promptly and fully from the postalcoholic syndrome without intervening delirium tremens. Subsequent maintenance doses of promazine, given orally, do not always produce sleep. When somnolence occurs, the patient is easily aroused and responds readily and alertly to questioning.

In our experience, promazine has proved highly effective for outpatient treatment of the postalcoholic syndrome after acute exacerbation of chronic alcoholism. The drug promptly controls severe withdrawal symptoms and abolishes tremulousness, hallucinosis, incontinence, nausea, and vomiting in the vast majority of alcoholic patients (more than 90% in our series). We feel the drug is safely administered orally, by private physicians, to the alcoholic patient in dosages of 100 mg. repeated every four hours as necessary. Promazine in our hands has demonstrated more merit than any other drug yet tested in ability to control the postalcoholic syndrome.

The efficacy of promazine reported here may encourage general hospitals to accept more alcoholic patients, even though they are acutely inebriated or exhibit severe abstinence symptoms. The calming influence of the drug should abolish the need for restraints. It should also obviate complaints from other patients or hospital personnel about boisterous or unmanageable alcoholics.

Summary

The postalcoholic syndrome is controllable on an outpatient basis. Administered orally, promazine hydrochloride abolished all symptoms of the postalcoholic syndrome in 229 of 243 (94%) chronic alcoholic patients in whom delirium tremens was not a complication. No side-effects were observed at the recommended dosage level.

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METHYLPHENIDATE HYDROCHLORIDE THERAPY AFTER ATTEMPTED SUICIDE

REVIEW OF THE LITERATURE AND REPORT OF A CASE

Evelyn Parker Ivey, M.D., Morristown, N. J.

Recent experience of successful treatment of a patient after an overdose of sedative demonstrated the effectiveness of parenterally given methylphenidate (Ritalin) hydrochloride in potentiating the pressor effect of levarterenol bitartrate, recognized to be a potent vasopressor drug in itself. This quality, in addition to the fact that methylphenidate is a central nervous system stimulant with a wide margin of safety, warrants the consideration of all physicians who administer large doses of sedatives or who treat patients after attempted suicide.

The patient, a 35-year-old woman, was found in a comatose state by her husband approximately six hours after having been observed in good health. By her side were empty bottles suggesting she had swallowed an unknown number of capsules of ethchlorvynol (Placidyl) and tablets of methyprylon (Noludar); the amount was later estimated as 9,000-10,000 mg. of the former and 14,000-18,000 mg. of the latter drug. The patient had been seen to drink alcoholic beverages copiously on the preceding evening. When discovered, she was mildly cyanotic, with shallow respirations and a slow, thready pulse. Her pupils were dilated and did not react to light. Corneal and deep tendon reflexes were absent.

Immediate treatment was instituted, consisting of gastric lavage followed by injection of a weak solution of magnesium sulfate, intravenously given caffeine and sodium benzoate, intranasal administration of oxygen, and cerebral stimulation with the use of an electrostimulating machine. The patient was placed in modified "shock position." An oral airway insured patency of the air passage. Frequent suction removed secretions from the pharynx to further facilitate breathing. An indwelling urethral catheter permitted easy flow and the collection of urine for measurement. Further initial supportive treatment consisted of continuous intravenous infusion of 5% glucose or fructose (Levugen) in water with vitamin B complex with C (Berocca C) and the administration as antibiotics of penicillin and sterile penicillin-dihydrostreptomycin for suspension (Combiotic). As the patient's condition progressed, tracheal intubation became necessary. Secretions from the tracheobronchial tree were meticulously aspirated by use of a catheter and suction apparatus. Swollen eyelids, chemosis, and rales in the lungs revealed the presence of edema. Intra-

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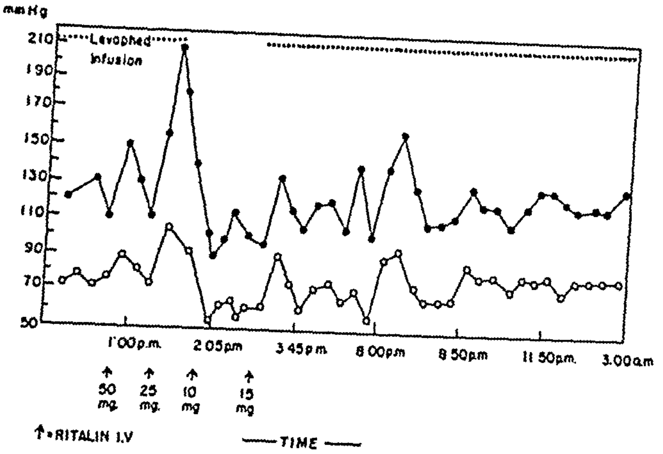
From the Morristown Memorial Hospital.

venous administration of 10% glucose in water replaced the previous solutions in the dehydration effort. Later in the course of treatment, it also became advisable to administer additional mineral salts solutions intravenously to counteract electrolyte deficits as determined by clinical and laboratory evaluations.

Despite the early supportive treatment and the use of electrostimulation, the patient's blood pressure continued to fall and became imperceptible within a short period of time. Intravenous administration of isotonic sodium chloride solution with levarterenol (Levophed) was helpful in elevating the blood pressure, but marked drops in pressure continued to occur. Blood pressure could be maintained only by increasing the rate of the intravenous drip of levarterenol, thereby increasing the danger of thrombosis of the small, collapsed veins. A dose of 50 mg. of methylphenidate, injected intravenously when the blood pressure was 110/72 mm. Hg, prompted an immediate rise to 150/90, followed by a slow return to the former level of 110. One hour later, 25 mg. of methylphenidate, given by intravenous injection, promptly stimulated a blood pressure change from 110/70 to 210/105 mm. Hg. The physicians, apprehensive of the sudden dramatic elevation of blood pressure, withdrew the levarterenol. The blood pressure began its decline. When it had reached 140/90 mm. Hg, an intravenous injection of 10 mg. of methylphenidate did not alter its course. It continued to fall, reaching 90/50, but then resumed a range of 100/60 to 110/70 mm. Hg. A subsequent injection of 15 mg. of methylphenidate did not affect this range of the blood pressure appreciably.



Potentiation of pressor action of levarterenol (Levophed) bitartrate by methylphenidate (Ritalin) hydrochloride, as determined in therapy after suicide attempt.

Meanwhile, the patient's condition appeared to be improving, so, after three hours, the intravenous administration of isotonic sodium chloride solution with levarterenol was resumed. This now proved to be effective in maintaining the blood pressure level. The figure shows the dramatic response of the blood pressure when methylphenidate was used during the course of the levarterenol infusion.

Comment

Maxwell and co-workers[1] have demonstrated the effect of methylphenidate in dogs to potentiate the pressor responses to epinephrine, levarterenol, and naphazoline hydrochloride. Plummer and Yonkman[2] have summarized the effect of methylphenidate on the circulatory system of the dog. They have emphasized that this agent is free of the pressor action of amphetamine, that it antagonizes the hypertensive effect of amphetamine and suppresses the pressor effect of ephedrine, but, in contrast, that it potentiates the pressor effect of levarterenol in dogs. They called special attention to the clinical import of these observations. To my knowledge, this potentiation of the pressor effect of levarterenol has not previously been reported in humans.

The patient reported on here had appeared moribund and remained in coma for about 45 hours. Medical evaluation and treatment as described above was continuous in an attempt to maintain the physiological and electrolyte balance. Electrostimulation, used during the first 14 or 15 hours, appeared helpful in maintaining respiration. Robie[3] and other workers have described the advantage of this treatment in stimulating respiration and have suggested its function in expediting the metabolism of the drug in the brain.

During the course of treatment, the patient developed a number of complications. A period of apnea occurred during the minimal electrostimulation; this responded to treatment with continued electrostimulation, artificial respiration, and pentylene tetrazol (Metrazol) administration. An anesthetist inflated the lungs at regular intervals as a further preventive measure against atelectasis. Despite this intensive medical treatment and supervision, however, atelectasis and bronchial pneumonia did develop, necessitating a tracheotomy. Subsequent additional complications of acute gastroenteritis and bilateral thrombophlebitis of the saphenous vein required continued active medical treatment, which was finally rewarded by the recovery of the patient.

The method of treatment of any comatose patient after an attempted suicide must be determined individually, based on careful medical observation with special attention to the vital functions. Eckenhoff and Dam[4] have concluded from the evidence available that supportive therapy is the method of choice in treating barbiturate poisoning. They state, "Analeptics appear to be without value and may even increase the hazard of narcosis by causing convulsions, cardiac irregularities, and vomiting." They regard analeptics as contraindicated when anoxia or hypoxia is present. These authors mention cerebral electrostimulation and hemodialysis as hopeful but as needing substantiation by study of larger series of patients.

Less is written about the treatment of the patient who has attempted suicide by taking large amounts of the nonbarbiturate sedative. At this hospital, the same general principles of treatment apply, but it appears to be more difficult to maintain the electrolyte balance. The early appearance of edema, detectable externally in the eyelids and internally on auscultation in the lungs, is characteristic. Central nervous system stimulants (amphetamines, pentylene tetrazol, and picrotoxin) may be indicated in acute respiratory failure but add potential hazards which must be considered.

Methylphenidate has been described as a "central stimulating drug with properties that lie somewhere between the amphetamines and caffeine, although chemically it is unrelated to either one of these preparations."[5] Its value in reducing the recovery time of patients from anesthesia has been reported by a number of observers. Gale[6] showed methylphenidate to be "useful in shortening recovery time after thiopental-nitrous oxide anesthesia" and suggested its value in counteracting "the respiratory and circulatory effects of anesthetic adjuvants." Smith and Adriani[7] wrote that this drug proved to be "more effective than the older analeptics in mild and severe barbiturate intoxication" and that it tends "to shorten the period of depression and reduce complications."

Carter and Maley[8] emphasized the safety of methylphenidate in a report on its use in patients with profound chronic brain damage; it had the effect of stimulating respiration and alerting consciousness. This effect occurred whether the indications within the damaged brain were shock from overdosage of chlorpromazine hydrochloride or reserpine, severe barbiturate poisoning, anesthesia, or the need for a stimulant in patients moribund from systemic disease. Ferguson[9] demonstrated the effectiveness of methylphenidate in relieving the feeling of depression and in counteracting the crippling aspects of the sedative effect of high doses of ataraxics in patients with no organic brain disturbance.

Conclusions

Parenterally given methylphenidate (Ritalin) hydrochloride, a central nervous system stimulant with a wide margin of safety, may provide an advantage in the treatment of patients who have taken an overdose of sedatives, barbiturate and nonbarbiturate. Its ability to potentiate the pressor response of levarterenol bitartrate suggests additional indications, as well as the need for caution, when the physician uses the two medicaments in combination.

24 Elm St.

The methylphenidate hydrochloride used in this study was supplied as Ritalin hydrochloride by Ciba Pharmaceutical Products, Inc., Summit, N. J.

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THE SUICIDE PROBLEM.—Coroners, of necessity, gather information to establish the cause of death rather than to understand the suicide. If more significant insights and knowledge about suicide are to be developed, systematic information needs to be gathered at the time of death. Such information about the suicide should include his developmental background, extent of education, stability of employment, income, health, history of previous psychiatric hospitalization including diagnosis of mental disorder, interpersonal relationships, pattern of adjustment, temperament, interests, stress situations, and whatever other factors that may be deemed important. Such information should be obtained not only from members of the family, relatives, and friends but also from more objective collateral sources, such as the family doctor and employer, and through search of court, hospital, and social agency records. . . . The majority of the suicides had been under medical supervision prior to their death, usually by the family doctor. This suggests that the family doctor is in a key position to recognize psychiatric problems in his patients at the earliest possible time and to refer them to appropriate psychiatric resources for special care and treatment. It would be helpful if material on the problem of suicide, with emphasis on methods of detecting individuals with suicidal tendencies, were introduced in the medical school curriculum.—Jacob Tuckman, Ph.D., and Martha Lavell, M.S.S., Study of Suicide in Philadelphia, *Public Health Reports,* June, 1958.

DIAGNOSTIC PROBLEMS

PRESENTATION OF CASE

John O. Archambeau, M.D., Chicago

A 56-year-old man was first hospitalized May 2, 1954, because of a change in his bowel habits and weight loss. His blood pressure was 150/80 mm. Hg, and his pulse rate 90 per minute. His heart sounds were of good quality, cardiomegaly was not noted, and the electrocardiogram (ECG) showed a left axis deviation with a minor intraventricular conduction defect. A roentgenogram of the chest was normal. A biopsy specimen was taken from a fungating tumor of the rectum which extended 4 to 14 cm. above the mucocutaneous junction. Histological examination revealed mucosecretory adenocarcinoma. A combined abdominoperineal resection was performed and examination of the specimen revealed metastases in 2 of 20 regional lymph nodes. After discharge he remained well for 18 months then was readmitted on Feb. 8, 1956, because of fracture of the right clavicle which contained a tumor mass measuring 9 by 6 by 6 cm. His blood pressure was 145/75 mm. Hg. Basilar rales and a nonproductive cough were noted. The heart was enlarged and an apical systolic murmur was heard. The ECG showed a left bundle-branch block and a supraventricular tachycardia. An anterior myocardial infarction could not be excluded. A roentgenogram of the chest revealed parenchymal infiltrations believed to be metastases and a cardiomegaly of 35% oversize. Histological examination of a biopsy specimen of the right clavicular mass showed it to be a metastasis.

The patient's condition remained unchanged until three days prior to his third admission on Feb. 28, when a severe, oppressive pain developed over the upper part of the abdomen, lower part of the chest, and the left side of his neck. He had associated dyspnea, restlessness, and ankle edema. The physical examination revealed an acutely ill man with rasping respirations. His blood pressure was 150/80 mm. Hg; pulse rate, 100; respirations, 24; and temperature, 38 C (100.4 F). He had bilateral inspiratory and expiratory basilar rales. The cardiomegaly had increased since the previous examinations. The heart sounds were distant and an apical friction rub was heard. The leukocyte count was 16,000 per cubic millimeter; the corrected sedimentation rate was 33 mm.; the ECG showed a sinus tachycardia, a right bundle-branch block, and findings compatible with, but not diagnostic of, myocardial infarction. On the second hospital day he had ventricular tachycardia, which was treated successfully with 0.4 Gm. of quinidine intravenously. He was maintained on oral doses of 0.4 Gm. a day of quinidine, but continued to have recurrent bouts of paroxysmal ventricular tachycardia. With bed rest and therapy with oxtriphylline (Choledyl), quinidine, and aspirin, his symptoms disappeared and he was discharged on the 14th hospital day.

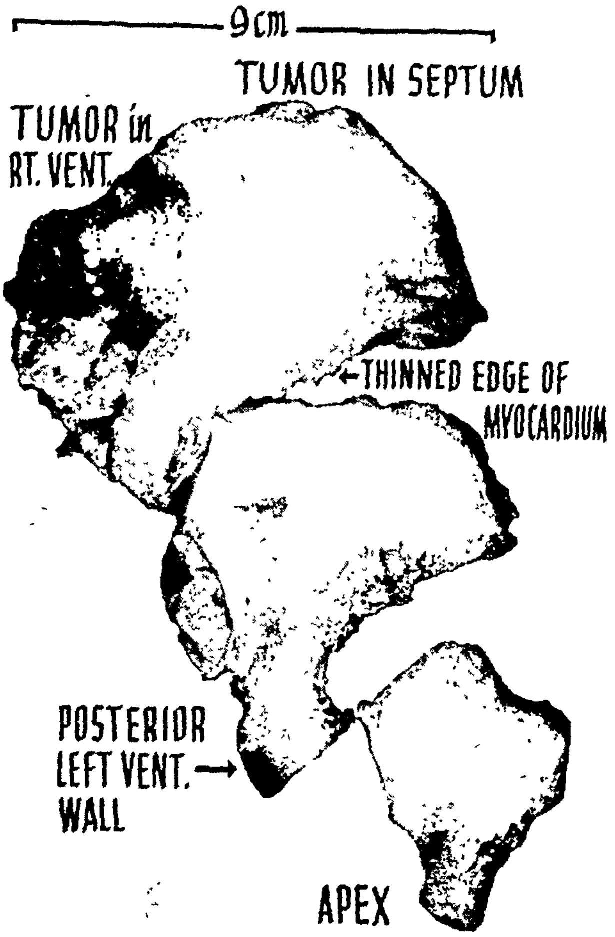

Fig. 1.—Transverse sections of three levels of interventricular septum showing massive tumor replacement. Only thin edge of uninvolved myocardium remains along left ventricular surface.

From the Department of Pathology, University of Chicago. Dr. Archambeau is now at the Tumor Institute of The Swedish Hospital, Seattle, as a Trainee, National Cancer Institute.

He remained weak, and clinically there was progression of his clavicular and pulmonary metastases; but he was able to return to part-time work until September. There was no recurrence of his chest pain, but the abdominal and right clavicular pain were troublesome. In September weakness, lassitude, and exertional dyspnea increased. Pedal edema developed and extended to the sacrum. He coughed more frequently, and the cough was productive of small amounts of bloody sputum. Anorexia was pronounced. On Nov. 20, he was readmitted. His blood pressure was 118/90 mm. Hg; pulse rate 88; and respirations 22. The clavicular mass had increased to 20 by 15 cm. Axillary and epitrochlear lymph nodes were palpable. Examination of the chest revealed decreased breath sounds and dulness to percussion. The heart had enlarged to percussion with the area of cardiac dulness extending 11 cm. from the sternum. Apical grade 2 presystolic and systolic murmurs were heard. Splenomegaly was noted. His leukocyte count was 6,700 per cubic millimeter, with a normal differential count. The hemoglobin level was 15.7 Gm. Microscopic examination of the urine showed pyuria and hematuria. The serum electrolyte levels were as follows: sodium, 136 mEq. per liter; potassium, 5.9 mEq. per liter; chlorine, 88 mEq. per liter; and carbon dioxide, 20.5 mM per liter. The alkaline phosphatase level was 8 units per 100 ml. The plasma protein levels were as follows: albumin, 4.1 mg. per 100 ml., and globulin, 2.9 mg. per 100 ml. The serum bilirubin level was 6.4 mg. per 100 ml. direct and 1.3 mg. per 100 ml. indirect. The cephalin flocculation test was 1+. The nonprotein nitrogen level was 46 mg. per 100 ml. A roentgenogram of the chest showed pleural effusion on the right side, a large mass in the posterior left lower lung field behind the heart, and almost complete destruction of the medial portion of the right clavicle. An ECG showed persistent right bundle-branch block. During this time the laboratory findings remained essentially unchanged. The patient became increasingly dyspneic even at rest and had to be placed in an oxygen tent. His abdominal and chest pain required increasing doses of analgesics and finally narcotics for relief. With digitalization his respiratory symptoms and anasarca improved temporarily, but his course was one of progressive deterioration and he died on the 31st day of hospitalization.

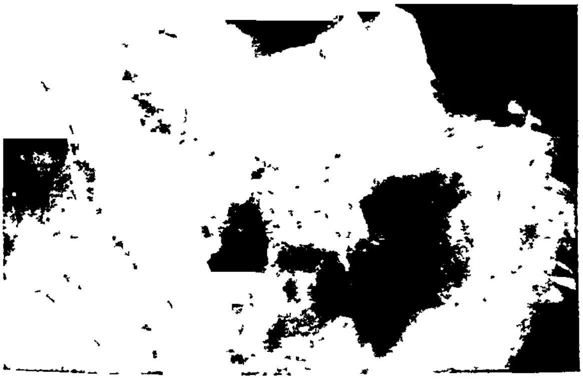

Fig. 2.—Pulmonary valve with projection of tumor from septal metastasis, partially obstructing pulmonary outflow.

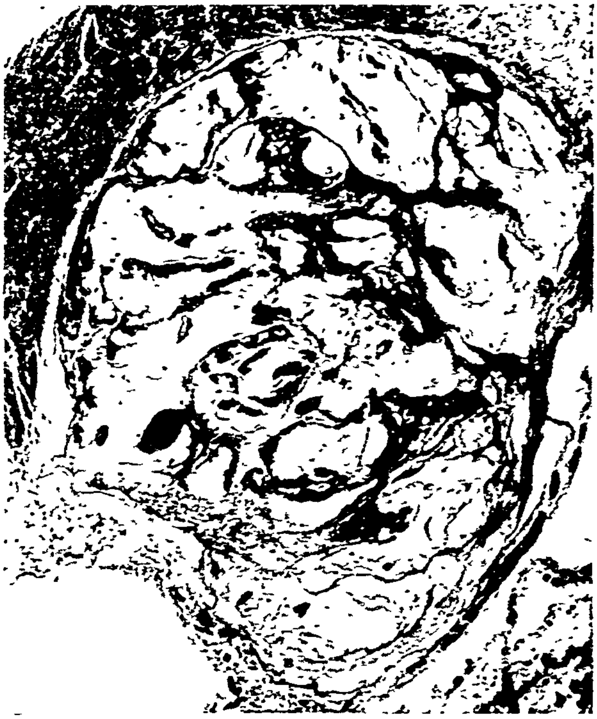

Fig. 3.—Section of coronary sinus obstructed by tumor extension from septum. Note large mucus lakes (× 18).

The final clinical diagnoses were carcinoma of the colon metastatic to the clavicle, lung, and liver and an old myocardial infarction.

Anatomic Diagnosis

The body was well-nourished, measured 69 in. (175.3 cm.), and weighed 172 lb. (78 kg.). Anasarca was marked, with a brawny edema of the face and neck. The anterior surface of the chest and neck were markedly congested. The large ovoid clavicular tumor mass measured 15 by 9 by 8 cm., replaced the whole clavicle, and extended into the sternum. The abdominal panniculus was 3 cm. thick. The peritoneal cavity contained 500 cc. of clear ascitic fluid. The 500-Gm. spleen with its huge tumor mass mechanically obstructed the colon. The 1,500-Gm. liver was small, firm, and atrophic, with no metastases. The left adrenal was replaced by tumor. Both kidneys weighed 200 Gm. and contained diffuse areas of metastatic tumor infiltration. There was 1,500 cc. of hemorrhagic pleural effusion on the right and 200 cc. on the left. The lungs were congested and edematous, and the posterior segment of the left lower lobe contained a single metastasis 9 cm. in diameter. A thromboembolus and adjacent area of infarction was found in the right upper lobe. The 900-Gm. heart measured 19 cm. in its greatest diameter. The interventricular septum measured 9 cm. across at its widest point and was nearly replaced by gelatinous, yellow-brown tumor (fig. 1). Only a thin line of uninvolved myocardium persisted on the ventricular surface of the left ventricle. The tumor extended from the apex to 1 cm. above the pulmonary valve, where a long projection of tumor and thrombus partially blocked the pulmonary outflow (fig. 2). Scattered myocardial tumor plaques were present in the anterior wall of the ventricle. Papillary muscles and chorda tendinae were severely involved. The aortic ring and aortic-pulmonary septum were involved. The coronary sinus (fig. 3) and left anterior descending coronary were completely obstructed and in areas replaced by tumor. Tumor surrounded segments of the left and right coronaries. The remaining myocardium was pale red-brown, soft, and friable. The valve rings were insufficient.

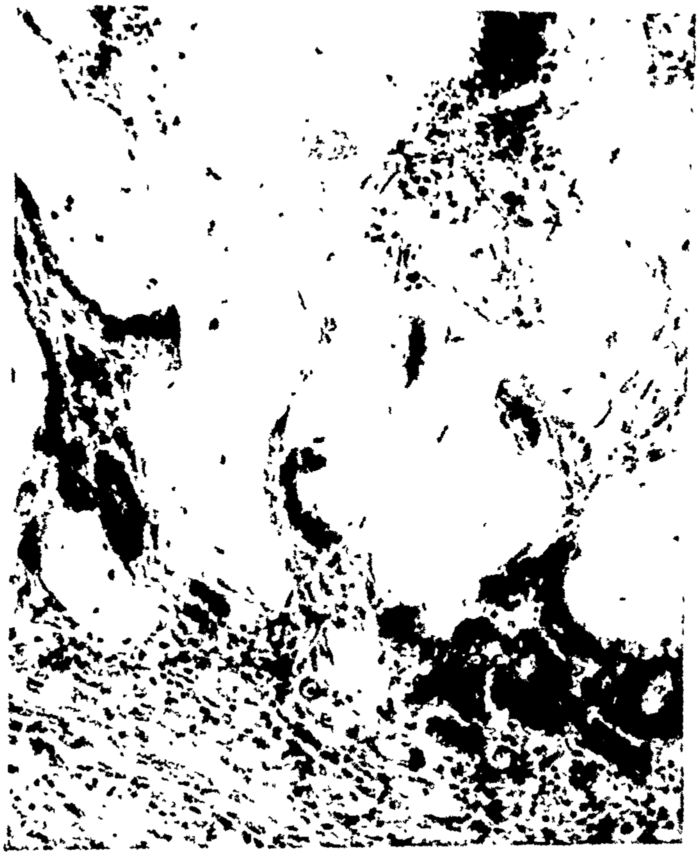

Fig. 4.—Section of periphery of septal metastasis showing mucus lakes, thinned stroma, glandular acini, and myocardial infiltration (× 180).

Histologically, the tumor was a mucosecretory adenocarcinoma with numerous mucus lakes and thinned fibrous stroma (fig. 4). The postmortem morphology was similar to that of the original surgical specimen. The sections of the heart confirmed the extensive myocardial replacement and the vascular and valvular invasion. The lungs, in addition to the single metastasis, contained multiple microscopic tumor emboli. The liver was free of tumor, and in addition to atrophy and fatty change had a mild inactive postnecrotic type of cirrhosis.

COMMENT

Fausto Tanzi, M.D., Chicago

Cardiac metastases are not rare. The heart or pericardium is found involved by metastatic tumor in 2 to 20% of patients with malignancy. Carcinoma of the breast, bronchogenic carcinoma, malignant melanoma, and malignant lymphomas are the most common primary tumors involving the heart. Metastatic involvement, however, has been reported from primary malignant lesions of almost any organ. Antemortem diagnosis of metastasis to the heart has been made in very few of these cases. In most instances, as in the present one, an antemortem diagnosis is of academic interest only. The recent advances in cardiac surgery may make surgical treatment possible in selected patients. Because of the frequency of this condition, it should be considered in a differential diagnosis. Unexplained sudden heart failure, arrhythmias, pericardial effusions, friction rubs, cardiac murmurs, and changing electrocardiographic patterns in a patient with a known malignancy should arouse strong suspicion. The clinician should then consider the advisability of further diagnostic procedures in those patients in whom an attempt at extirpation of the tumor may seem justified.

It is apparent from the record of this patient that his myocardium was able to respond to digitalization, with improvement of the congestive heart failure, even in the presence of the severe metastatic involvement. Adequate doses of quinidine might have controlled the arrhythmia, although this is difficult to ascertain. A diagnosis of metastatic involvement of the heart should not necessarily mean that the patient should be denied a thoughtful consideration of the possible advantages of either medical or surgical therapies.

From the Department of Medicine, University of Chicago.

COMMITTEE ON COSMETICS

Report to the Committee

The effects of the sun on the skin are of medical interest because of the serious implications to both health and skin appearance of single and repeated overexposure. In previous reports (J. A. M. A. 161:1480 [Aug. 11] 1956; ibid. 161:1565 [Aug. 18] 1956), the Committee has concerned itself primarily with ways and means of minimizing effects of the sun on the skin through a regimen of moderate exposure supplemented by topically applied preventives. It is with interest that the Committee views the introduction of an orally administered drug which is claimed to provide sunburn prevention and to accelerate and accentuate tanning. This is significant because presently available topically applied preparations are effective in screening out portions of the sun's burning rays, but they do not in any way alter an individual's inherent ability to tan. Because of widespread interest in the cosmetic usefulness of this new drug, the Committee has authorized publication of the following report.

VERONICA LUCEY CONLEY, *Secretary.*

SUNTANNING—POTENTIATION WITH ORAL MEDICATION

Marion B. Sulzberger, M.D., New York
and
Aaron B. Lerner, M.D., Ph.D., New Haven, Conn.

It was known from the ancient folk-medicine practiced by the natives of Egypt that derivatives of the plant Ammi majus Linn could restore pigment in vitiliginous skin areas. In 1947 Fahmy and Abu-Shady[1] isolated the most active agents from extracts of this plant. They initiated clinical studies which confirmed the native lore by demonstrating that both internal administration and external application of the plant extractives, when combined with exposure to sunlight, did indeed bring about repigmentation in certain patches of vitiligo.[2] Further confirmation of these facts was soon forthcoming in Egyptian publications and in the European and American literature.[3] The most active pigment-stimulating ingredients of the plant were found to be in the group of natural furocoumarins, compounds long known to possess photosensitizing properties. Among these compounds are the oxypsoralens. A good deal of the recent work in the United States has been done with methoxsalen (Meloxine, Oxsoralen), also known as 8-methoxypsoralen or 8-MOP.

Use of Methoxsalen for Vitiligo

Experience with the oxypsoralens has established the principle that they, plus repeated exposure to natural or artificial ultraviolet rays in the wave lengths from 2500 A to 3660 A and perhaps higher, can induce pigment formation in certain areas of vitiligo. Experience also has shown that the vitiligo problem is far from solved. The clinical response is erratic and unpredictable, and cosmetically satisfactory repigmentation can be obtained in only about one out of every seven patients treated. In some cases the repigmentation may be permanent; in others repeated courses of treatment may be necessary. Moreover, repetition of the courses of treatment does not always bring about the same beneficial effect. The treatment is long, tedious, and time consuming—each course requiring months to years of exposure to ultraviolet rays, from either lamps or natural sunlight, daily or at least several times weekly. Local application of the psoralens, probably the most pigment-stimulating form of their use, has been almost entirely abandoned because of the severe edema, erythema, blistering, and pain that can be produced when the skin is subsequently exposed to natural or artificial ultraviolet rays. Side-reactions experienced by patients receiving methoxsalen orally include nausea, epigastric distress, diarrhea, increased nervous tension, headache, and depression. On the other hand, the original fear that methoxsalen might cause liver damage has not been proved in a single case.[4]

Because of the difficult and time-consuming nature of this therapy and its small and unpredictable yield of satisfactory clinical results in vitiligo,

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From the Department of Dermatology and Syphilology, New York University Post-Graduate Medical School, New York University–Bellevue Medical Center (Dr. Sulzberger) and the Section of Dermatology, Department of Medicine, Yale University School of Medicine (Dr. Lerner).

it is not to be wondered that dermatologists are far from satisfied with the method as over-all treatment of this disease. Furthermore, many patients do not wish to undergo the long series of treatments once the outline and prospects of therapy have been clearly explained to them. Despite these drawbacks, it is by far the best treatment for vitiligo at the present time.

Use of Methoxsalen for Tanning and Light Protection

The origin of an entirely different field of usefulness, namely, the idea of using methoxsalen to increase the general tanning of the skin for cosmetic purposes as well as to increase the general tolerance of the sensitive skin to sunlight, stems from relatively recent observations.[5] A physician's wife being treated for vitiligo observed that ingestion of methoxsalen before exposure to sunlight substantially enhanced the tanning response of her normal-appearing skin. This finding has been confirmed repeatedly, and the drug has been recommended as an aid to suntanning.[5] The medical profession must now decide whether to endorse the systemic use of this drug solely for light protection and cosmetic tanning in a large and not easily controllable segment of the population. The following pertinent questions come to mind as having direct bearing on this decision. Just how effective is this drug in increasing suntanning and tolerance to light? By what mechanisms does it achieve these effects? What are its side-effects? Is it safe for general use, continuously or repeatedly through many years?

Effectiveness of Drug.—The first question, that of efficacy for potentiating suntanning and sun tolerance, can be answered as follows. Despite a recent report showing that the degrees of hyperpigmentation are often not very obvious or readily discernible clinically,[6] most investigators agree that the skin of many normal persons, as well as the normally pigmented areas of many patients with vitiligo, develops some increase over the normal hyperpigmentation when repeatedly exposed to sunlight within two to four hours after ingestion of 10 to 20 mg. of methoxsalen. Moreover, some sun-sensitive subjects, including albinos, state that their skin has acquired increased tolerance to sunlight while they were taking methoxsalen. However, for achieving this effect the dosage both of drug and of sun exposure is a delicate one. For, if the first exposures to sunlight are a little too long or if the dose of methoxsalen is increased to 30 to 70 mg. daily instead of 10 to 20 mg. daily, a reaction the opposite of that desired may take place; that is, all cutaneous reactions to ultraviolet rays become accentuated, so that erythema, edema, blistering, and pain occur.

Mechanisms of Action.—Recently progress has been made concerning the second question, that of mechanisms of action. S. W. Becker Jr.[7] has studied the histological changes in the skin which occur after chronic oral administration of psoralens and exposure to ultraviolet radiation in normal persons (20 mg. of methoxsalen daily given two hours before exposure to ultraviolet rays). He finds that the most prominent change is a thickening of the horny layer of the skin, resulting in an extremely compact layer. He also finds the formation of a stratum lucidum, a layer below the stratum corneum which normally is seen only where the horny layer is physiologically very thick, as on the palms and soles. In consonance with the findings of Guido Miescher[8] on sun protection in general, it is this increased density and thickness of the stratum corneum which appear to be largely responsible for the increased resistance of the skin to sunburn after psoralen therapy. The natural insensible desquamation of such a thickened and compact horny layer is diminished. According to Becker, the diminution of shedding plays a role in the increased darkening of the skin after psoralen administration. Normally, pigment granules ascend in the epidermis and are cast off with the desquamating horny lamellae. In a compact thickened horny layer this "excretion" of melanin dust is considerably slowed down. Therefore, such skin appears darker. In Becker's presentation, if there is increased melanin formation under the combined influence of psoralens and sunshine, this is in correlation with the inflammation produced, that is, the greater the inflammation, the greater the pigment production. However, an increased tanning is achieved mainly by *retention* of melanin. The adherent stratum corneum retains the pigment which reaches it. In addition, a large amount of melanin is retained also in the basal-cell layer.

It is interesting to note that formation of a compact thickened horny layer is a rather common reaction to a great variety of insults to the skin, one being repeated exposure to ultraviolet rays. Possibly this traumatic effect of ultraviolet radiation is being exaggerated by psoralens because these compounds are powerful photosensitizers.

Potential Toxic Effects.—Although present experience indicates that most healthy adults can safely take 10 to 20 mg. of methoxsalen daily by mouth for one to two weeks to increase their tolerance to sunlight or to obtain more tanning, there still remain many unknowns. Thus, it is not known in what ways protracted or repeated ingestion of methoxsalen may affect patients with gastrointestinal disease, liver disease, or chronic infection. Moreover, concerning cutaneous ill-effects, it is not yet known what will happen to the skin when courses of methoxsalen and sun exposures are repeated once or twice or oftener each year for many years and a deeper than normal tan develops.

Will the incidence of basal-cell or squamous-cell carcinomas be changed, either decreased or increased? Will other senile skin changes be delayed or accelerated? Will there be any effect on the formation of melanomas? Mice exposed to ultraviolet rays for long periods of time develop cutaneous carcinomas. When selected strains of mice are injected intraperitoneally with given quantities of methoxsalen daily throughout an experimental period, the incidence of carcinomas is increased.[9] Yet, if they receive the drug orally, the incidence of carcinomas is decreased.[9] How will these effects produced in mice compare with those which may be produced in man? Which dose and route of administration may prove to enhance carcinogenesis and which to reduce carcinogenesis in the skin of man? These are some of the questions which the medical profession must consider before endorsing the oral ingestion of this drug—not for the treatment or prevention of a disease but for normal fair-skinned persons who burn excessively or for normal persons with adequate pigment who desire a tan for cosmetic purposes alone.

Comment

Recognizing and stimulated by the importance of questions such as these, early in the spring of 1958, a group of investigators held a major conference on various aspects of sun radiation. In this conference the therapeutic effects and potential toxic effects of methoxsalen were thoroughly discussed on the basis of the experimental data available. The detailed proceedings of this conference will appear at a later date in the *Journal of Investigative Dermatology*. However, it can be stated now that no unequivocal answers to the questions we have propounded could be given on the basis of any of the findings reported up to the present.

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ROLE OF QUININE IN HEMOLYSIS.—Intravascular haemolysis of erythrocytes during quinine administration is met with clinically in cases of blackwater fever. There is considerable controversy about the aetiology of blackwater fever. It is now generally accepted that it is caused by infection due to Plasmodium falciparum and that administration of quinine and pamaquin precipitates an attack (Fairley and Murgatroyd, 1940). Innumerable instances from the literature can be cited where patients did not get haemoglobinuria until they had received a large dose of quinine; should the patient recover from the effects of the fever, a second dose of quinine may produce haemoglobinuria again. Fairley and Murgatroyd (1940) reported a case where four attacks occurred in one patient following the administration of quinine. Thus quinine under certain circumstances can cause haemolysis, but its mechanism of action has not been elucidated.—R. S. Grewal, The Role of Quinine in Haemolysis, *British Journal of Pharmacology and Chemotherapy*, June, 1958.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Cable Address . . . . "Medic, Chicago"

CORTICOSTEROIDS, ACTH, AND INFECTIONS

INFECTIOUS diseases in general are characterized by inflammation, fever, and a toxic state.[1] Antibiotics and the sulfonamides have been used successfully to stop the growth of the invading organisms but they do not stop the inflammatory reaction. Adrenocorticosteroids and corticotropin, hereinafter referred to simply as hormones, have no antimicrobial action but do reduce the inflammatory reaction and induce a feeling of well-being. For this reason many attempts have been made to combine antimicrobial and hormonal therapy, but unfortunately the hormones cause undesirable side-effects when used *in large doses for a long time.* They may activate peptic ulcers or interfere with the body's defense mechanism. Kass and Finland[2] stated that when hormones are used in conjunction with antimicrobial agents the former reduce the effectiveness of the latter thus necessitating increasing the dose of the antibiotics. Vascular collapse is one of the most serious complications of severe infection and against this complication hormonal therapy can be helpful.

Ribble and Braude[3] stated that in pneumococcic meningitis an inflammatory reaction is of little value to the patient if a bactericidal drug is used because the leukocytes speed up the destruction of bacteria only if the bacteria are multiplying. They treated 12 patients who had pneumococcic meningitis with antimicrobial agents and hormones. Only one patient died. This gave a recovery rate of 92%, or more than would be expected from treatment with antimicrobial agents alone. The survivors showed no deleterious effects of hormonal therapy. Spink[1] has suggested the use of the hormones in patients having vascular collapse due to infections caused by gram-negative bacteria (epidemic cerebrospinal meningitis). These include infections due to Meningococcus, Salmonella, Brucella, Proteus, Pseudomonas, and Klebsiella. The hormones should be administered along with pressor agents, such as levarterenol or metaraminol, and antibiotics. Peerman and McGanity[4] were able to relieve 10 patients who had had long-standing pelvic inflammatory disease by giving cortisone and chlortetracycline. In a follow-up ranging from three months to two years there were no recurrences.

One of the most important uses of hormones is as an adjunct in the treatment of selected patients with tuberculosis. This subject was ably discussed by Des Prez and Organick[5] who stated that in this disease the reaction of the host to his infection actually impedes the action of the new chemotherapeutic agents and favors the development of drug-resistant strains. Here again the hormones are of benefit only when used in conjunction with antituberculosis drugs. Such treatment decreases fever and toxicity and increases the patient's appetite and feeling of well-being. Radiologic improvement can also be demonstrated. In patients with tuberculous meningitis this combined treatment gives clinical improvement, prevents subarachnoidal block, and may even reverse an early block. It also reverses abnormalities of the spinal fluid. Thus it may prevent a permanent disability or even save life. Patients who could not take antituberculosis drugs because of a hypersensitivity were able to

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take them without difficulty when concomitant hormonal treatment was given. The authors found no proof that combined treatment in patients with uncomplicated pulmonary tuberculosis was any better than treatment with antituberculosis drugs alone. When hormones were indicated they found little difference between treatment with cortisone and treatment with ACTH but their results slightly favored the latter. They recommended doses of 20 to 80 units a day for one to three months. Hormonal treatment should be discontinued as soon as the treatment objectives are obtained but withdrawal must be gradual in the case of cortisone or its derivatives and at the end of the course the adrenals should be stimulated with a short course of ACTH. When properly used hormones do not interfere with the development of the immune reactions. Hormones must never be given to a patient who is infected with a strain of organisms resistant to antituberculosis drugs.

In patients undergoing treatment for leprosy a lepromatous reaction to the sulfones may occur. Hormones control the acute reaction but are less effective against a chronic reaction. As in the case of tuberculosis, hormones may make it possible to continue treatment with specific drugs to which a patient shows a hypersensitivity. Hormones may also prevent permanent nerve damage in patients with acute leprous neuritis.[6] In patients with infectious mononucleosis in whom thrombocytopenia, severe involvement of the central nervous system, or hemolytic anemia occur hormones have been beneficial.[7] They have also helped patients with severe viral hepatitis who were not benefited by conventional measures. Zeluff and Fatherree[8] used hormones with gratifying results in four patients with mumps orchitis. A much larger series was reported by Petersdorf and Bennett[9] who warned that hormones are not a preventive of this complication. All of their patients obtained prompt relief and no untoward effects were noted. Patients with measles encephalitis were similarly improved. When the hormones were withdrawn some patients relapsed but were cured with a second course. Postvaccinal encephalitis recurring after smallpox and rabies vaccination has also been treated successfully with hormones.

No drug should be given unless one can be reasonably sure that it will benefit the patient. Hormonal agents when given over a brief period to patients critically ill with an infectious disease will often bring about a dramatic improvement without harmful side-effects and may prevent death or permanent disability. They should not be used for mild or moderate infections and should be given usually only if an effective antimicrobial drug is given at the same time.

SUNTANNING

A new and challenging problem now faces the medical profession with the introduction of a drug for cosmetic purposes alone. Within the coming year physicians may be required to appraise the usefulness and safety of methoxsalen, which is being offered to the profession as a drug to accentuate and accelerate tanning of the normal skin.

Since time began, man has had to devise ways and means to protect himself from the sun. In temperate climates this was not a serious problem, except for those whose occupations demanded prolonged exposure. However, since the social significance of a tanned skin has made it a desirable commodity, sunbathing has become a major leisure time activity for a large segment of our population. Consequently, a wide market exists for externally applied sunscreens which, if properly used, permit tanning while minimizing uncomfortable and disfiguring burns. It can be postulated that there is an even greater demand for a preparation which, when taken internally, produces effects beyond those of present suntan preparations; namely, to increase a person's usual tanning capacity by mere ingestion of a pill which does not make the skin sticky, oily, or dry or have any of the drawbacks which cannot be avoided from topical application or whose effects do not wash off.

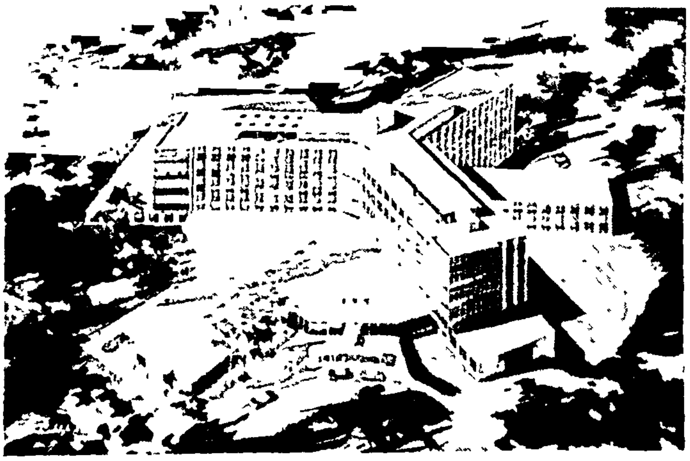
It is against this background that Drs. Marion B. Sulzberger and Aaron B. Lerner report to the Committee on Cosmetics on "Suntanning—Potentiation with Oral Medication" which appears in this issue of The Journal, page 2077. These dermatologists discuss the status of methoxsalen in the treatment of vitiligo and severe intolerances and hypersensitivities to sunlight (i. e., albinos) and favor its continued medical use and prescription for these purposes in properly selected cases. They point out the major differences between the use of this drug for diseases and disabilities under medical supervision and its use for purely cosmetic reasons by a large and not easily controlled segment of the population. The cosmetic effectiveness of the drug, systemic side-effects, and chronic toxicity have not been completely studied. No one knows what will happen to the skin when courses of methoxsalen and sun exposures are repeated once, twice, or oftener each year for many years. Nor is it yet certain what effects, good or bad, this drug will have on the development and course of skin malignancies or on the usual senile skin changes. Any physician endorsing the systemic administration of this drug for the cosmetic goal of acquiring a "beautiful tan" must do so with full realization of the many unknowns, the potential dangers always to be considered when large numbers of persons take an active systemic medicament for long periods of time without regular medical examination, and the fact that even the esthetic value of its effects is still dubious.

ORGANIZATION SECTION

"TOMORROW HOSPITAL" UNDERGROUND

A New Jersey hospital project which combines concepts of progressive patient care (Medicine At Work, THE JOURNAL, April 26, 1958, p. 2180) with those of survival under catastrophe is being studied by federal and medical observers. It is the new St. Barnabas Medical Center which will be built on ground now being cleared at Livingston, N. J., 10 miles from the present St. Barnabas, Newark's oldest hospital (incorporated in 1867).

The 60-acre site at Livingston has been approved by the Office of Defense and Civilian Mobilization, which is watching developments closely to see whether this distinctive design may represent a showpiece of what can be done in hospital construction for both war and peace. Also studying the project are staff members of the A. M. A. *Committee on Civil Defense, under the Council on* National Defense. According to George C. Schicks, D. Sc., St. Barnabas executive secretary who designed the facility in collaboration with the architectural firm of Ferrenz & Taylor, the 650-bed medical center will cost 10 to 12 million dollars when it is completed in 1960, and will function primarily around an underground "core."



Architect's drawing of proposed new St. Barnabas Medical Center at Livingston, N. J., designed as "hospital of tomorrow for war and peace." Heart of 650-bed facility, embodying principles of progressive patient care, lies in two underground floors. Plan is approved by civil defense authorities.

Underground construction was decided upon when the contractor determined it would cost no more than erecting above ground, and probably less. This was discovered by Swedish engineers 10 years ago, and today Sweden's largest hospital has fully equipped underground facilities.

"There has been too much talk but little action to solve many hospital administration problems," Dr. Schicks said last week. "In formulating our plans we have visited the modern hospitals in many parts of the United States—and while each fits certain needs, none seemed to strike at the basic problems. The St. Barnabas plan represents the eighth we have considered since we first asked architects to 'draw us up a hospital.' We feel that the demand for a hospital of this sort is apparent and the need is imperative."

Details of Layout

The projected St. Barnabas Medical Center is two stories below ground and four stories above. However, the upper floors are composed almost entirely of convalescent wards. The functioning nucleus of the hospital is below street level, where there will be operating rooms, intensive care units and emergency facilities. Ambulances, six at a time, could unload at underground ramps. There, too, will be outlets from deep water wells, and—when the development is refined—a nuclear power plant. Also below ground will be shelter areas to protect patients as well as the able-bodied members of the community from the effects, even, of above-ground fall-out. Thus might the hospital be a self-sustaining unit in wartime or peacetime disaster.

Separate wings for admission, intensive care, and convalescence are to be arranged so that, for example, a patient ready for surgery never would come in contact with a patient whose appearance or condition may be emotionally disturbing. Nursing services will be concentrated in the intensive care units, thereby saving many patients up to $50 a day in fees that otherwise might be paid to special-duty nurses, according to Dr. Schicks. He estimates that the new hospital should be able to care for one-third more patients than at present, without increasing the number of personnel.

"Keeping Well People Well"

The St. Barnabas Medical Center is expected to serve 250,000 persons in 25 surrounding communities—inviting them into the hospital to take part in a full-scale health education program. This will be in the hands of physicians, nurses, and skilled technicians and will include public forums, live demonstrations, and the use of films and television. The plan also calls for taking these educational tools into the surrounding communities, with the aim "to reduce one's chances of being the one person in eight who will become a hospital patient this year."

Dr. Schicks estimates that if this sort of progressive care reduces the patient's hospital stay by only one day, the Blue Cross saving in New Jersey alone would be $5,460,000 and, projected to hospitals throughout the U. S., $85,000,000. He adds that if the present figure of one-in-eight persons hospitalized becomes one in nine (through better health education) the reduction in cost for Blue Cross would be $1 million for New Jersey and $100 million for the nation. "Since Blue Cross writes half of the health-hospital service policies," Schicks said, "the potential annual saving to all insurance plans or companies in the United States would approach $370 million. This saving could be passed on to subscribers in reduced rates or to help keep premiums stabilized. It is possible that the 'hospital of tomorrow' can make these reductions in cost a reality."

PHYSICIANS' REGISTRATION AT SAN FRANCISCO MEETINGS

JUNE 21-25, 1954	
Alabama	43
Alaska	5
Arizona	109
Arkansas	30
San Francisco	
California (incl. San Francisco)	6,553
Colorado	130
Connecticut	47
Delaware	9
District of Columbia	136
Florida	100
Georgia	46
Hawaii	45
Idaho	38
Illinois	523
Indiana	178
Iowa	86
Isthmus of Canal Zone	3
Kansas	97
Kentucky	40
Louisiana	85
Maine	6
Maryland	101
Massachusetts	120
Michigan	229
Minnesota	184
Mississippi	18
Missouri	157
Montana	30
Nebraska	91
Nevada	50
New Hampshire	11
New Jersey	90
New Mexico	46
New York	389
North Carolina	50
North Dakota	21
Ohio	320
Oklahoma	63
Oregon	230
Pennsylvania	284
Puerto Rico	6
Rhode Island	15
South Carolina	38
South Dakota	30
Tennessee	63
Texas	313
Utah	99
Vermont	25
Virginia	108
Washington	255
West Virginia	49
Wisconsin	106
Wyoming	15
TOTAL	11,915

JUNE 23-27, 1958	
Alabama	46
Alaska	7
Arizona	82
Arkansas	32
San Francisco	1,507
California	5,711
Colorado	120
Connecticut	56
Delaware	8
District of Columbia	113
Florida	144
Georgia	67
Hawaii	56
Idaho	38
Illinois	506
Indiana	169
Iowa	100
Isthmus of Canal Zone	4
Kansas	91
Kentucky	73
Louisiana	100
Maine	8
Maryland	119
Massachusetts	126
Michigan	205
Minnesota	163
Mississippi	32
Missouri	162
Montana	24
Nebraska	68
Nevada	56
New Hampshire	11
New Jersey	147
New Mexico	48
New York	472
North Carolina	73
North Dakota	23
Ohio	334
Oklahoma	78
Oregon	217
Pennsylvania	293
Puerto Rico	4
Rhode Island	21
South Carolina	27
South Dakota	23
Tennessee	102
Texas	399
Utah	98
Vermont	2
Virginia	68
Washington	308
West Virginia	43
Wisconsin	132
Wyoming	23
TOTAL	13,029

OTHER COUNTRIES

1954	
Argentine	7
Australia	1
Austria	1
Bahamas	1
Brazil	1
Canada	73
Costa Rica	2
Cuba	4
Denmark	1
England	5
Finland	1
France	2
Germany	2
Guam	1
India	3
Iran	2
Iraq	4
Israel	1
Italy	2
Japan	4
Korea	3
Mexico	7
Netherlands	1
Philippine Islands	9
Portugal	2
South Africa	2
Spain	1
Sweden	2
Switzerland	2
Thailand	1
TOTAL	148
GRAND TOTAL	12,063

1958	
Africa	3
Argentine	7
Australia	2
Austria	3
Belgium	1
Brazil	1
Canada	64
Chili	4
China	2
Colombia	1
Cuba	7
Denmark	3
East Africa	1
Egypt	1
El Salvador	1
England	17
France	4
Germany	2
Guam	2
Guatemala	1
Holland	1
Iceland	1
India	7
Indonesia	2
Iran	1
Israel	1
Italy	1
Japan	10
Korea	2
Lebanon	2
Mexico	15
Nicaragua	1
Pakistan	1
Philippine Islands	2
Scotland	2
South Africa	3
Sweden	3
Switzerland	1
Thailand	3
Venezuela	1
Virgin Islands	1
West Africa	1
TOTAL	189
GRAND TOTAL	13,218

PHYSICIANS' REGISTRATION COUNT BY SECTIONS

Anesthesiology	300
Dermatology & Syphilology	275
Diseases of the Chest	291
Experimental Medicine & Therapeutics	77
Gastroenterology & Proctology	177
General Practice	2,736
Internal Medicine	1,766
Laryngology, Otology & Rhinology	310
Military Medicine	187
Nervous & Mental Diseases	394
Obstetrics & Gynecology	601
Ophthalmology	529
Orthopedic Surgery	351
Pathology & Physiology	308
Pediatrics	444
Physical Medicine & Rehabilitation	74
Preventive & Industrial Medicine & Public Health	224
Radiology	333
Surgery, General & Abdominal	1,333
Urology	268
Session on Allergy	40
Session on Legal Medicine	12
No section checked	1,033
Total	12,063

Anesthesiology	374
Dermatology & Syphilology	277
Diseases of the Chest	284
Experimental Medicine & Therapeutics	84
Gastroenterology & Proctology	125
General Practice	2,418
Internal Medicine	1,747
Laryngology, Otology & Rhinology	242
Military Medicine	134
Nervous & Mental Diseases	380
Obstetrics & Gynecology	502
Ophthalmology	513
Orthopedic Surgery	377
Pathology & Physiology	289
Pediatrics	500
Physical Medicine	52
Preventive Medicine	214
Radiology	350
Surgery, General & Abdominal	1,191
Urology	229
Session on Allergy	50
Session on Injury in Sports	10
Session on Medical Professional Liability	14
Session on Traffic Accidents	10
More than one section checked	189
No section checked	2,663
Total	13,218

FEDERAL MEDICAL LEGISLATION

85th Congress

Aging and Handicapped

S. 3700, by Senator Langer (R., N. D.), would establish a 10-man United States Commission on the Aging and Aged. Six members (three from federal agencies and three from private life) would be appointed by the President—two Senators and two Representatives. The commission would study existing programs of aid to the aged with respect to employment, income maintenance, health and physical care, housing, living arrangements and family relationship, and effective use of leisure time. It would solicit cooperation from the various professional, business, and labor groups which are concerned with problems of the aged. The commission would have the right to hold hearings and require information and records, by subpoena, from individuals and organizations and would also have the right to obtain data from other federal agencies.

S. 3701, by Senator Langer, would create, as an independent agency, the Federal Agency for Handicapped. All of the functions of the Department of Health, Education, and Welfare under the provisions of the Vocational Rehabilitation Act and under the public assistance program to assist the blind and several of the functions of the Department of Labor would be transferred to the new agency. In addition to the carrying out of all of the existing programs of federal departments, there would be added many additional federal programs to aid the handicapped. These would include (*a*) a loan program to states to establish cooperative enterprises for handicapped persons; (*b*) amendment of the act that gives blind persons a priority in the operation of vending stands in federal buildings to give preference also to other handicapped persons, such as those suffering from cerebral palsy, cardiac conditions, arthritis, epilepsy, and other diseases; (*c*) a broadened program of federal assistance to states in the operation of rehabilitation centers; (*d*) a new program of federal assistance to states in aiding special programs for the severely handicapped; (*e*) initiation of a revolving loan fund from which state programs could make loans pending appropriations from their legislatures for carrying on rehabilitation programs; (*f*) establishing a Division for the Handicapped in the U. S. Civil Service Commission to give assistance to handicapped persons in procuring federal employment; (*g*) creation of a "Federal Second Injury Tax and Fund" to require every employer (employer is defined as any person required under state workmen's compensation laws to issue disability benefits to his employees) to pay to such fund an excise tax equal to one-tenth of one per cent of total wages which has as its purpose the removal of barriers to the employment of handicapped persons in industry; (*h*) creation of a commission to survey and determine proper selection placement of handicapped individuals; (*i*) provide federally-aided interpreters for the deaf and other physically handicapped persons who are litigants before federal courts, departments, agencies, or congressional committees; (*j*) authorization for earmarked appropriation to be used as grants to states to finance special schooling and education services to those handicapped commonly known as "shut-ins" (In this program the federal government would design and apply a pilot program to cover three states. Mobile training units, which would include medical services, would render assistance to the handicapped.); (*k*) establishment in the Labor Department of a Committee for the Training and Development of Placement Personnel. Grants could be made by this committee to colleges and universities and public and private agencies to establish courses of instruction to improve the competency of qualified personnel to work with the handicapped; (*m*) establishment of a federal program of grants to the states for aiding those unfeasible of rehabilitation. Disabled persons would be provided with payments of $60 per month, and periodic medical examinations not less than one year apart would be required.

S. 3702, by Senator Langer, would establish a temporary National Advisory Committee for the Blind, composed of nine members appointed by the President, to study existing federal, state, and local activities related to the granting of services to the blind. The committee would be charged with making a report with recommendations to the President and Congress within 24 months after passage of the act. The bill authorizes the committee to hold hearings and to secure information from any executive department, bureau, or other government agency; power to subpoena witnesses is included. The sum of $100,000 is authorized to finance the expenses of the project. The committee would cease to exist 30 days after it submitted its report and recommendations to the President and Congress.

H. R. 12051, by Representative Libonati (D., Ill.), is identical to H. R. 383, by Representative Rhodes (D., Pa.), and H. R. 11057, by Representative Zablocki (D., Wis.), which would provide for the establishment of the Bureau of Older Persons within the Department of Health, Education, and Welfare and would authorize federal grants to assist in the development and operation of studies and projects to help older persons.

Construction

S. 3713, by Senator Clark (D., Pa.) and others, is identical to H. R. 12327, by Representative Addonizio (D., N. J.), which would amend the Hous-

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From the Washington Office of the American Medical Association.

ing Act of 1950 to authorize 250 million dollars to be used in making loans, bearing interest equal to that paid by the United States (approximately 3%), to colleges for the construction of classrooms, laboratories, and related facilities (including initial equipment), and for the rehabilitation, alteration, and improvement of existing structures. An educational institution is defined "as any institution offering at least a two-year program acceptable for full credit toward a baccalaureate degree, including any public educational institution, or any private educational institution no part of the net earnings of which inures to the benefit of any private shareholder or individual." This definition would not include teaching hospitals. To qualify for a loan the college would have to show its inability to secure funds from other sources at comparable terms to those provided in the Housing Act. Loans could not exceed the cost of land and construction as determined by the Housing Administrator.

H. R. 12187, by Representative Clark (D., Pa.), is identical to S. 3497, by Senator Fulbright (D., Ark.) and others, as passed by the Senate, and H. R. 12492, by Representative Gray (D., Ill.). It provides a one billion dollar loan program for the construction of community facilities, bearing interest equal to that paid by the United States (currently 3.5%). Among the eligible facilities for which loans may be made are public and nonprofit hospitals. To be eligible, a nonprofit hospital would be required to meet the standards of the Hill-Burton program and be certified to that effect by the surgeon general. The program would be administered by the Housing and Home Finance Administration.

Public Health Service

S. 3724, by Senator Magnuson (D., Wash.), would amend the present law which currently provides that seamen employed on vessels of the United States registry are entitled to medical, surgical, and dental treatment and hospitalization without charge at public health hospitals so that eligibility would be extended to "any person employed or engaged on board." A number of Congressmen have sought a more liberal interpretation of the law in recent years so that masters and owners of vessels could be accorded the same privileges as employed seamen.

S. 3727, by Senator Purtell (R., Conn.), would authorize the surgeon general to encourage and assist in international activities for the "promotion of health and the prevention and conquest of disease, including the conduct of investigations, research and demonstrations . . . and the dissemination and exchange of health information," and to "authorize [him] to serve . . . as the national health administrator for the purposes of any international commitment of the United States." The bill also provides that the surgeon general may provide services in support of such activities subject to the approval of the Secretary of State and may detail personnel of the Public Health Service to international organizations.

H. R. 12100, by Representative Rhodes (R., Ariz.), is identical to H. R. 12134, by Representative Westland (R., Wash.), which would provide for the construction, improvement and extension of certain sanitation facilities for Indians. This bill would authorize the surgeon general of the Public Health Service to obtain, from the secretary of the interior, federal or government-controlled, Indian-owned lands for the purpose of constructing, improving, or extending community water supplies and facilities, drainage facilities, and sewage and waste disposal facilities for the benefit of Indian tribes. The surgeon general is also authorized to transfer such facilities to any state or territory or subdivision thereof or to any Indian tribe, group, band, or community.

H. R. 12331, by Representative Knutson (D., Minn.), would require the surgeon general to undertake a special research program with respect to cystic fibrosis and would authorize an appropriation of $200,000 for research by the National Institutes of Health in this field. These funds would be in addition to any other funds for medical research in this field provided by existing law. The surgeon general would also be authorized to use the funds to recruit and train individuals to conduct research in this field.

Social Security

H. R. 12007, by Representative Coad (D., Iowa), would amend the Social Security Act for disability insurance benefits and the disability freeze in the case of certain individuals. This bill would liberalize the requirements for the disability freeze or disability benefits for those individuals brought under the social security system by the 1954 and 1956 amendments to the law, by temporarily eliminating the requirement of coverage for 5 of the 10 years preceding disability, until sufficient time has passed for the individuals to qualify.

H. R. 12033, by Representative Libonati (D., Ill.), H. R. 10532, by Representative Dellay (D., N. J.), H. R. 12173, by Representative Patterson (R., Conn.), and H. R. 12300, by Representative Santangelo (D., N. Y.), are identical to H. R. 9467—the Forand Bill.

H. R. 12493, by Representative Boggs (D., La.), would increase the amount of benefits payable under the federal old-age survivors and disability insurance program. This bill would provide a 10% or $5 increase (whichever is more) in the monthly money benefits paid under the social security program. To finance these increases, the tax rate on the present wage base of $4,200 would be increased. On Jan. 1, the tax would be increased for the self-employed from the present $141.75 to $157.50; in 1975 the tax would reach $309.75. For the employed, the present tax of $94.50 would be increased to $105.00, and by 1975 the employer and employee would each pay $183.75 under the proposed changes.

H. R. 12050, by Representative Libonati (D., Ill.), is identical to H. R. 8883, by Representative Kean (R., N. J.), which would amend the Social Security Act to provide, among other things, compulsory coverage of physicians, benefits for dependents of disabled workers, payment for rehabilitation services, and increased benefits to workers who delay retirement.

H. R. 12503, by Representative McIntosh (R., Mich.), would liberalize requirements for disability benefits under social security by eliminating the age 50 requirement for eligibility for disability cash payments. Thus, any disabled individual who could meet the coverage requirements would be entitled to the monthly cash benefits for disability. In addition, the bill would reduce the retirement age under the social security program from 65 years to 62 years.

H. R. 12504, by Representative McIntosh (R., Mich.), would amend the Social Security Act to redefine the term "disability" in establishing entitlement to disability insurance benefits. This bill contains virtually identical provisions of two bills introduced by Representative Dingell. This bill, compared with H. R. 10578, by Representative Dingell (D., Mich.), would redefine the term "disability." Under existing law an applicant for disability benefits or the freeze is eligible only if he is found unable to engage in any substantial gainful employment because of a physical or mental impairment. Under this bill, if the applicant could not obtain employment in an occupation similar to the work he engaged in prior to the onset of disability, he would be eligible for disability payments or freeze benefits.

Compared with H. R. 10583, the bill by Representative McIntosh also provides that the existence of a qualifying disability would be conclusively proved for both disability benefits and freeze benefits if the applicant submits a statement from a federal or state agency that his disability is permanent and total under the agency's definition and that the agency is paying or has paid cash benefits for such disability.

S. 3771, by Senator Langer (R., N. D.), and H. R. 12528, by Representative Blatnik (D., Minn.), are identical to H. R. 11678, by Representative O'Neill (D., Mass.), which would amend the public assistance provisions of the Social Security Act to add a fifth category of recipients—needy persons not eligible for assistance under the present four programs of aid.

H. R. 12568, by Representative Anfuso (D., N. Y.), would provide an increase in all benefits payable under social security by 40% and to lower the retirement age for men and women to 62 years. To meet the cost of this liberalization, increased tax rates would be imposed on the present wage base of $4,200. On Jan. 1, the tax would be increased for the self-employed from the present $141.75 to $362.25; in 1975 the tax would reach $488.25. For the employee and employer, the present tax of $94.50 would be increased to $241.50, and by 1975 the employer and employee would each pay $325.50 under the proposed changes.

Taxes

H. R. 12035, by Representative Libonati (D., Ill.), is identical to S. 3194, by Senator Sparkman (D., Ala.) and others, and would amend the Internal Revenue Code of 1954 so as to establish an initial program of tax adjustment for small and independent business and for persons engaged in small and independent business; it includes a Jenkins-Keogh type tax deferment proposal.

H. R. 12042, by Representative Libonati, is identical to H. R. 10394, by Representative Matthews (D., Fla.), and would amend the Internal Revenue Code of 1954 to eliminate present provisions which restrict medical expense deductions to the excess of 3% of taxpayer's adjusted gross income.

Veterans' Affairs

H. R. 12056, by Representative Siler (R., Ky.), would amend the Veterans' Benefits Act of 1957 to prohibit the reduction of service-connected disability ratings which have been in effect for 10 or more years, except upon showing that the rating was based on fraud. It would also provide that such disability which has been in effect for 10 or more years and which has been reduced within that period shall not be reduced any further thereafter. The bill also provides that a veteran whose 10-year disability rating had been reduced in the past could have the original rating restored by applying for such action to the Administrator of Veterans Affairs.

H. R. 12096, by Representative Abernethy (D., Miss.), would provide for peacetime veterans a 3-year presumption of service-connection for active tuberculosis resulting in 10% degree of disability or more.

H. R. 12383, by Representative Addonizio (D., N. J.), would increase the period of presumption of service-connection for veterans suffering from multiple sclerosis from the present two year to seven years from date of separation from service.

Health, Education, and Welfare

H. R. 12166, by Representative Lankford (D., Md.), is identical to H. R. 11714, by Representative Blatnik (D., Minn.), and would amend the Water Pollution Control Act to increase one of the limitations on grants for construction and for other purposes from $250,000 to $500,000.

H. R. 12338, by Representative Teller (D., N. Y.), would have the same effect as S. 2888, by Senator Douglas (D., Ill.) and others, which passed the Senate on April 28, in that it would require the reporting to the Secretary of Labor of information dealing with welfare and pension plans by labor unions. The bill specifies what type of information shall be filed and provides penalties for failure to comply.

H. R. 12190, by Representative Engle, is identical to H. R. 10730, by Representative Sheppard (Democrats, Calif.), and would amend the public assistance provisions of the Social Security Act to provide increased payments and eliminate certain restrictions.

Miscellaneous

Reorganization Plan no. 1 of 1958, introduced by the President, would merge the functions of the Office of Defense Mobilization and the Federal Civil Defense Administration in a new agency to be known as the Office of Defense and Civilian Mobilization. All functions of the two agencies would be vested in the President, and the new Office would be made part of the Executive Office of the President. The plan provides for a director, deputy director, and three assistant directors to be appointed by the President, by and with the advice and consent of the Senate. It also provides for up to 10 regional directors. The President would be authorized to delegate civilian defense functions to any federal agency. On this point, there is some question as to exactly which functions the President would delegate, save, or eliminate. Unless the plan is rejected by a simple majority of either the House or Senate within 60 days of the above transmittal date, it will become effective on July 1, 1958. (The plan became effective on July 10. Governor Hoegh, former director of FCDA, is the new director.)

S. Res. 297, by Senator Potter (R., Mich.), is a resolution directed against the Reorganization Plan no. 1 of 1958 and reads as follows: "That the Senate does not favor the Reorganization Plan Numbered 1 of 1958 transmitted to the Congress on April 24, 1958."

H. R. 12524, by Representative Reed (R., N. Y.), would discontinue federal grants for vocational education and waste treatment facilities and would reduce the federal excise tax on local telephone service to assist the states in assuming financial responsibility for these programs.

The purpose of this bill is to return to the states the responsibility for vocational education and water pollution control. To meet the cost of these programs, the states would be expected to tax local telephone service. Under existing law, federal tax paid by the user is 10%. A tax credit equal to the amount of the state tax or 40% of the present federal tax, whichever is less, would be granted to taxpayers in the states which impose such a tax to carry out the programs. The authorization for tax credits would continue until July 1, 1964. At that time the federal tax on local telephone service would be reduced to 6%. It is assumed that by July, 1964, all the states would have imposed a 4% tax on local telephone service. The bill also provides for the repeal of federal laws dealing with vocational education and the repeal of the grant-in-aid section of the Water Pollution Control Act of 1956.

H. R. 12541, H. R. 12542, and H. R. 12543, by Representatives Vinson (D., Ga.), Kilday (D., Texas), and Arends (R., Ill.), respectively, would promote the national defense by providing for reorganization of the Department of Defense.

This is a new bill reported by the House Armed Services Committee to accomplish the reorganization of the Department of Defense. While the bill differs from the Administration's bill with respect to the chain of command and operations of the various services, its language concerning the Assistant Secretaries of Defense is identical to the Administration's bill. It makes no specific recommendations concerning the Assistant Secretary of Defense for Health and Medical. This bill has already passed in the House and is now under consideration by the Senate.

Indications are that the Administration will abolish the office of the Assistant Secretary of Defense for Health and Medical and relegate it to that of a special assistant to the Secretary of Defense.

THE BILL OF RIGHTS FOR THE COLLEGE ATHLETE

Participation in college athletics is a privilege involving both responsibilities and rights. The athlete has the responsibility to play fair, to give his best, to keep in training, to conduct himself with credit to his sport and his school. In turn he has the right to optimal protection against injury as this may be assured through good technical instruction, proper regulation and conditions of play, and adequate health supervision. Included are:

Good Coaching: The importance of good coaching in protecting the health and safety of athletes cannot be minimized. Technical instruction leading to skillful performance is a significant factor in lowering the incidence and decreasing the severity of injuries. Also, good coaching includes the discouragement of tactics, outside either the rules or the spirit of the rules, which may increase the hazard and thus the incidence of injuries.

Good Officiating: The rules and regulations governing athletic competition are made to protect players as well as to promote enjoyment of the game. To serve these ends effectively the rules of the game must be thoroughly understood by players as well as coaches and be properly interpreted and enforced by impartial and technically qualified officials.

Good Equipment and Facilities: There can be no question about the protection afforded by proper equipment and the right facilities. Good equipment is now available and is being improved continually; the problem lies in the false economy of using cheap, worn out, outmoded, or ill-fitting gear. Provision of proper areas for play and their careful maintenance are equally important.

Good Medical Care: Good medical care includes, first, a thorough preseason history and physical examination. Many of the sports tragedies which occur each year are due to unrecognized health problems. Medical contraindications to participation in contact sports must be respected. Second, a physician present at all contests and readily available during practice sessions. It is unfair to leave decisions to a trainer or coach as to whether an athlete should return to play or be removed from the game following injury. In serious injuries the availability of a physician may make the difference in preventing disability or even death. Third, medical control of the health aspects of athletics. In medical matters, the physician's authority should be absolute and unquestioned. Today's coaches and trainers are happy to leave medical decisions to the medical profession. They also assist in interpreting this principle to students and the public.

American Medical Association
Committee on Injury in Sports.

FOOD FADDISM

Four departments of the American Medical Association, in cooperation with one private and one federal agency, have joined in a program to alert the public to notorious health lecturers, worthless or harmful tonics and food supplements, phony health foods, and related false advertising claims. One project is an exhibit entitled, "Nutrition Nonsense and False Claims," which features an actual recording of the "pitch" made by a door-to-door salesman of food supplements.

The exhibit, to be completed this fall, is being prepared by the Council on Foods and Nutrition, the Bureau of Exhibits, the Public Relations Department, and the Bureau of Investigation—working with the National Better Business Bureau, and the Food and Drug Administration. A film entitled "The Medicine Man," dealing with the health lecturer who promotes his product as a cure-all of disease, is scheduled for release to television stations on Sept. 15. It will be previewed at the annual PR Institute in Chicago on Aug. 28.

Details of the program were related at a meeting of the Council on Foods and Nutrition in San Francisco last June by Dr. Philip L. White, Secretary of the Council. At that same meeting a committee was appointed, headed by Dr. David B. Hand of Geneva, N. Y., to prepare a statement defining low-fat and moderate-fat diets and give indications of their use.

A Hollywood actor, Dabbs Greer, portrays a witch doctor in the A. M. A.'s educational television film, "The Medicine Man." He bones up on the real thing in this photograph made during production. The film exposes nutrition fakers and is scheduled for release to television stations on Sept. 15.

The Council has authorized the preparation of symposium of brief articles for The Journal on certain controversial subjects in the field of foods and nutrition. The first series will discuss the significance of lowered cholesterol levels. Meanwhile, preparations are being completed for the Council's annual fall symposium to be held Oct. 16 at Madison, Wis., in cooperation with the university's medical school, the Dane County Medical Society, and the State Medical Society of Wisconsin. The subject is, "Factors Involved in Formation and Disease of Bone." Three symposiums are scheduled for next year. These include the regular fall session; another scientific symposium in the spring, at Vanderbilt University on the topic of lipids and fat-soluble vitamins; and a question-and-answer-period during the A. M. A. Annual Meeting next June in Atlantic City.

NEW INTERPROFESSIONAL MEDICOLEGAL CODE

A new code designed to improve relationships between physicians and attorneys was adopted by the American Medical Association's House of Delegates at its recent annual meeting in San Francisco. This "National Interprofessional Code for Physicians and Attorneys" was developed by the Joint Liaison Committee of the American Bar Association and the American Medical Association. The same code will be presented for approval to the Board of Governors and the House of Delegates of the American Bar Association at its meeting in August.

Dr. Gunnar Gunderson, A. M. A. President, and Charles S. Rhyne, American Bar Association President, discuss the new interprofessional code for physicians and attorneys prepared by the A. M. A.-A. B. A. Joint Liaison Committee.

The preamble states that it "will serve its purpose if it promotes the public welfare, improves the practical working relationships of the two professions, and facilitates the administration of justice."

The wording of the code has been kept general to allow its adaptation to local conditions. Various sections cover such topics as medical reports; conferences between the physician and the attorney; subpoena for medical witness; arrangements for court appearances; physician called as witness; fees for services of a physician relative to litigation; implementation of the code at state and local levels; and consideration and disposition of complaints by a member of either profession.

TEST FOR FOREIGN GRADUATES ON SEPTEMBER 23

At least 800 physicians in the United States and in 32 nations abroad are expected to take part Sept. 23 in the first world-wide qualification examination offered by the new Educational Council for Foreign Medical Graduates. More than half of the examinees will take the all-day test in centers set up at some 20 medical schools in the United States, according to Dr. Dean Smiley, executive director of the Council.

The Sept. 23 examination will consist of 126 questions in medicine, 90 in surgery, 54 in obstetrics and gynecology, 54 in pediatrics, and 36 in the basic sciences. This examination contains 40 fewer questions than the total which confronted 298 candidates in the first test given last spring at United States centers. A passing score was achieved by 152 of those examinees.

According to statistical data of the Council, a British medical school graduate was top scorer in last spring's test, correctly answering 367 out of 400 questions. One graduate of a Mexican medical school and another of a Swiss medical school each answered 364 questions correctly. Also among the top scorers were graduates of Latvian, Italian, Egyptian, Belgian, Chinese, and Hungarian medical schools. Leading by country in number of applicants were 35 graduates of German medical schools, of whom 21 attained passing scores; in contrast, two out of three Argentine medical school graduates passed. The best showing was made by graduates of Swiss medical schools, seven out of eight of whom passed; only one out of six Japanese graduates attained a passing score. The candidates ranged in year of medical school graduation from 1921 to 1958. However, two out of every three were graduated in the decade of 1947-1956. Similar examinations are to be given twice annually—next year in February and in September.

The Educational Council for Foreign Medical Graduates (located at 1710 Orrington Ave., Evanston, Ill.) is not a placement agency but rather a certifying organization. Tests are given only to candidates whose credentials are acceptable—at least 18 years of formal education, including 4 academic years in a bona fide medical school. Those who pass are certified as possessing medical knowledge reasonably equivalent to that expected of graduates of approved medical schools in the United States and Canada and as having satisfactory facility with the English language. Certification then may be transmitted to hospitals, licensing authorities, specialty boards, and other appropriate organizations.

MEDICAL NEWS

CALIFORNIA

Microradiographic Lab at UCLA.—A microradiographic laboratory for taking tiny x-ray pictures of microscopic tissue has been established at the University of California at Los Angeles Medical School. The new unit is under the direction of Richard C. Greulich, Ph.D. Techniques are based on the same principles as those of conventional x-ray imaging. However, very fine-grained photographic emulsion is necessary for the high resolution required to distinguish adjacent regions of altered mass or chemistry. The specimen must be in a vacuum so that the low-energy x-rays can penetrate air molecules sufficiently to produce a good negative. The microradiograms are about the size of a postage stamp and are examined in the light microscope.

Dr. Shaw Named Pediatric Head.—Dr. Edward B. Shaw, San Francisco pediatrician, has been appointed professor of pediatrics and chairman of the department at the University of California School of Medicine, San Francisco. Dr. Shaw has been a volunteer member of the school's part-time clinical staff since 1921 and is leaving private practice to devote full time to university service. Since 1928 he has been chairman of the department of communicable diseases at Children's Hospital in San Francisco. As chairman of the department of pediatrics, Dr. Shaw succeeds Dr. William C. Deamer, who intends to devote more time to research and teaching.

DISTRICT OF COLUMBIA

Department of Medical and Dental Illustrations.—Since its organization in 1954, the department of medical illustrations and photography of the Georgetown University School of Medicine has enlarged its scope and facilities. Recently a decision was made to offer the services of the department to the dental profession, and the name of the department was changed to include dental illustrations. The mission of the department is to create visual material applicable to publication and to teaching in medicine and dentistry. The facilities of the department are available to the medical and dental professions of the community as well as to the faculties of Georgetown's schools.

KANSAS

Meeting on Schizophrenia and Hospital Treatment Programs.—The Osawatomie State Hospital, Osawatomie, has announced that an Institute on Chronic Schizophrenia and Hospital Treatment Programs will be held Oct. 1-3, supported by a grant from the National Institute of Mental Health, Bethesda, Md., and Smith, Kline & French Laboratories, Philadelphia. The purpose of the meeting is "to define specific practical treatments of chronic schizophrenia for mental hospitals, to promote new ideas and research activity, and to debate, discuss, and clarify divergent points of view on schizophrenia." Presentations will be made on psychoanalytic ideas, communication theory, the viewpoint of social psychiatry, "intrusion" theory, the biological standpoint, and large-scale hospital programming. There will be individual and panel discussions. Participants will include: Dr. Karl A. Menninger, Topeka, Kan.; Dr. Nathaniel S. Apter, Chicago; Mr. Gregory Bateson, Palo Alto, Calif.; Dr. John H. Cumming, Kansas City, Kan.; Austin M. Des Lauriers, Ph.D., Topeka, Kan.; Dr. Jordan M. Scher, Baltimore, Md.; Dr. Otto A. Will Jr., Rockville, Md.; Dr. Bruno Minz, Paris; Ludwig von Bertalanffy, Ph.D., Los Angeles; Dr. Ian L. W. Clancey, Weyburn, Saskatchewan; Dr. Elmer F. Galioni, Stockton, Calif.; S. Kirson Weinberg, Ph.D., Chicago; Martin Scheerer, Ph.D., Lawrence, Kan. There is no registration fee, but attendance will be limited. For information write Dr. George Zubowicz, Superintendent, Osawatomie State Hospital, Osowatomie, Kan.

MASSACHUSETTS

Reactor for Medical Research.—The first tour of the reactor at the Massachusetts Institute of Technology was conducted Aug. 5 by Theos J. Thompson, LL.D., director of the reactor and professor of nuclear engineering at the institute. The new facility, which cost 3 million dollars, will be used primarily for research and training nuclear engineers. A feature of the construction is the medical therapy room located beneath the reactor core, available to physicians in the Boston area for treatment of patients. Other uses of the reactor will include research in biology and food technology. Medical facilities at the reactor were made possible by a $250,000 grant from the Rockefeller Foundation.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Personal.—John F. Enders, Sc.D., professor, Harvard Medical School, Boston, and Nobel Prize winner, received an honorary doctor of science degree from Western Reserve University, Cleveland, June 11.—— Claus B. Bahnson, Ph.D., of Littleton, who came to America from Denmark in 1954, is the first person ever appointed to the faculty of both Boston University's School of Medicine and School of Fine and Applied Arts. Sponsored by the Scientific Exchange Program of the American-Scandinavian Foundation and the U. S. State Department, he was appointed research associate in the department of psychiatry of Boston University's School of Medicine and is a visiting professor of piano literature and teaching associate in piano at the university's School of Fine and Applied Arts.

MISSOURI

Inpatient Psychiatric Service Program.—A special preopening tour Aug. 1 marked the completion of construction of the new 35-bed adult inpatient psychiatric service of the Jewish Hospital of Saint Louis. Jointly sponsored by the hospital and the Psychoanalytic Foundation of Saint Louis, the tour provided an opportunity for psychiatrists, physicians, and health agency representatives to inspect the new treatment facilities. The new program will be a "private, intensive treatment service designed to provide treatment facilities and meet the specialized needs of patients requiring depth psychotherapy under long-term hospitalization." An approach called the "therapeutic community," characterized by high patient-nurse ratio, will be used. The foundation has granted the Jewish Hospital $5,000 toward this program. The service will be under the direction of Dr. Irwin Levy, director of the hospital's department of neuropsychiatry. Dr. William D. Cone will be administrator of the program.

NEBRASKA

Begin Psychiatric Institute in Omaha.—Construction of a three-floor addition to the Nebraska Psychiatric Institute of the University of Nebraska College of Medicine, Omaha, began in July. Two floors will be devoted to neuropsychiatric research while the third will house a special facility for mentally retarded children, to be known as the Carl and Caroline Swanson Children's Clinic. The new facilities reportedly will allow the institute to expand its neuropsychiatric research program and to develop a program of service, training, and research in mental retardation. A psychiatric nursery is being added to the existing Children's Service. Total cost of the addition is $506,000, of which $55,150 was received from the Carl and Caroline Swanson Foundation, $150,000 from an anonymous donor, $59,000 from the University of Nebraska and the State Board of Control, $200,000 from the Health Research Facilities branch of the National Institutes of Health, and $41,850 from Hill-Burton funds.

New York City

Center for Study of Heart Diseases.—A center for the all-purpose treatment and study of heart diseases will be opened this winter at New York Medical College, Flower and Fifth Avenue Hospitals. The program to be known as the "cardiopulmonary program," will coordinate all services available to the heart patient in every department, with surgical, medical, and psychiatric teams working as one. A new operating room will be constructed and will include a control room for a team consisting of cardiologist, physiologist, electronic engineer, and anesthesiologist who will be able to offer guidance to the surgeon throughout an operation. The operating table will be equipped with electronically controlled audiovisual devices to record all vital processes. The surgeon, guided by specialists in the control room, can also glance at a wall screen which will give facts on the patient's condition. Electronic apparatus will relay the operation to a lecture room for training of heart surgeons. Dr. Leo M. Taran, who will serve as coordinator and director, has had postgraduate training in Berlin and Wiesbaden. Plans are being made for any heart patient, regardless of his financial status, to receive benefits of the cardiopulmonary program at New York Medical College.

TENNESSEE

Tennessee Valley Assembly Meets in Chattanooga.—Sponsored by the Chattanooga and Hamilton County Medical Society, the Tennessee Valley Medical Assembly will be held Sept. 29-30 at the Read House, Chattanooga. A film, "Stress and the Adaptation Syndrome," will be presented by Dr. Hans Selye, Montreal. Dr. Francis L. Chamberlain, San Francisco, president-elect of the American Heart Association, will present "Treatment of Hypertension" the morning of Sept. 30. The program includes the following speakers: Dr. Owen H. Wangensteen, Minneapolis; Drs. William R. Arrowsmith and Merrell O. Hines, New Orleans; John L. Parks, Washington, D. C.; Paul E. McMaster, Los Angeles; E. Perry McCullagh, Cleveland; Vincent J. Collins, New York City; McLemore Birdsong, Charlottesville, Va.; Manuel E. Lichtenstein and Herbert Rattner, Chicago; John R. Snavely, Jackson, Miss.; Kenneth W. Warren and Richard H. Overholt, Boston; Robert B. Greenblatt, Augusta, Ga.; Julian M. Ruffin, Durham, N. C.; William A. Altemeier, Cincinnati; Waltman Walters, Rochester, Minn. At the banquet Sept. 29, 7 p. m., Dr. Philip Thorek, associate professor of surgery, University of Illinois, Chicago, will speak on "Food for Thought." Registration fee is $15. For information write Dr. William G. Stephenson, Tennessee Valley Medical Assembly, 109 Medical Arts Building, Chattanooga 2, Tenn.

Appoint Head of Department of Dermatology.—Dr. Emmett R. Hall, head of the department of dermatology at the University of Tennessee College of Medicine since 1933, has been relieved of his administrative duties, but continues to serve as professor of dermatology. He has been succeeded by Dr. Vonnie A. Hall, who will be advanced from associate professor to professor and head of the department. He is a nephew of Dr. Emmett Hall.

VERMONT

Rehabilitation Center in Burlington.—The Vermont Rehabilitation Center is being constructed in Burlington with $325,000 voted by the Vermont State Legislature and $200,000 of federal (Hill–Burton) matching funds. The center was planned as a three-story building; however, a fourth story for clinical research has been added as a result of a National Institute of Health grant. The function of the center is "to furnish a focal point for a statewide attack on chronic illness and disability." It brings a full rehabilitation team in the immediate vicinity of the Vermont College of Medicine and connected with one of that college's two teaching hospitals, DeGoesbriand Memorial Hospital, to be used for teaching and to provide specialist treatment for the patient. The patient may carry out part of his program in his home area or he may take advantage of the facilities of the center. He will be followed on a regular periodic basis. Features of the center include a developing speech and hearing unit with a program which will integrate with the programs of the state agencies and with a curriculum for speech and hearing therapists. A cardiac or classification unit is functioning at the present time under subsidy from the Vermont Heart Association in combination with the cardiopulmonary unit of the DeGoesbriand Memorial Hospital. The Rehabilitation Center will be operated by the hospital. It is anticipated that another wing, a 60-bed long-term illness unit, will be added within a year.

VIRGINIA

Conference on Mental Retardation.—The Lynchburg Training School and Hospital in Colony will hold a conference on research and training in the field of mental retardation Sept. 11-12, made possible by a grant from the U. S. Public Health Service. The following topics will be presented at three sessions, "Research in Neurology," "Research and Training in Psychiatry and Social Work," and "Research and Training in Nursing, Psychology, and Education":

The Role of Modern Neurological Research Techniques in the Field of Mental Retardation.
Research Plans Dealing with Progressive Deteriorating Diseases and a Summary of an Analysis of 400 Autopsies on Institutionalized Patients.
The Development and Functional Organization of the Brain as Revealed by the Study of Malformations.
Preadmission Service.
Psychotherapeutic Considerations in the Treatment of the Mentally Retarded.
Training of Professional Personnel.
Basic Research on Learning in Mental Retardates.

All sessions will be held in the H. Minor Davis School Auditorium. No registration fee will be charged. For information write Dr. Benedict Nagler, Superintendent, Lynchburg Training School and Hospital, Colony, Va.

WASHINGTON

Dr. Blandau Wins Award for Sterility Study.—Dr. Richard J. Blandau, assistant dean of the University of Washington School of Medicine, Seattle, has been named winner of a national award by the American Society for the Study of Sterility, in Los Angeles. He received the Rubin award for "the most significant contribution to study in this field" for his work in studying the way the developing embryo is implanted in the uterus. Dr. Blandau also won this award in 1954 for previous studies. He is professor of anatomy at the medical school.

WISCONSIN

Appoint Director of Department of Surgery.—Dr. Edwin H. Ellison, associate professor of surgery, Ohio State University College of Medicine, Columbus, has been appointed professor and director of the department of surgery at Marquette University School of Medicine, Milwaukee, effective July 1. He replaces Dr. Carl W. Eberbach, who will continue in the teaching program of the medical school and will remain in the private practice of surgery. Dr. Ellison will be in charge of the educational and research programs in surgery for the Medical School at Milwaukee County Hospital and the Veterans Administration Hospital, Wood, and at Milwaukee Children's Hospital he will assist and guide the expansion of the undergraduate teaching program in pediatric surgery. Dr. Ellison was certified by the American Board of Surgery in 1954.

General Practice Meeting in Milwaukee.—The 1958 scientific assembly of the Wisconsin Academy of General Practice will be held Sept. 14-16 at the Milwaukee Auditorium. Dr. Theodore J. Nereim, president of the state academy, will open the meeting with an address. Four panel discussions are planned: Diabetes, Geriatric Problems, Congestive Heart Failure, and Medical Hypnosis in General Practice. The program includes the following papers by out-of-state participants:

Orthopedic Knee Injuries, Dr. Donald R. Lannin, St. Paul.
Cause and Prevention of Cystocele and Rectocele, Dr. J. Robert Willson, Philadelphia.
Management of Varicose Veins and Complications, Dr. Herman O. McPheeters, Minneapolis.
(1) Acute Infections of the Urinary Tract; (2) Hematuria—Diagnosis and Treatment, Dr. Louis K. Mantell, Waco, Texas.
Office Surgery, Dr. Paul S. Williamson, Dickenson, Texas.
Putting Science Across for Health, Chauncey D. Leake, Ph.D., Columbus, Ohio.
Delivery Room Emergencies, Dr. Mitchell J. Nechtow, Chicago.

For information write Dr. Edgar M. End, 758 N. 27th, Milwaukee 8, Wis., Secretary.

GENERAL

Psychosomatic Society Meets in Atlantic City.—The American Psychosomatic Society will hold its 16th annual meeting at Chalfonte-Haddon Hall in Atlantic City May 2-3, 1959. The Program Committee would like to receive titles and abstracts of papers for consideration for the program no later than Dec. 1. The time allotted for presentation of each paper will be 20 minutes. Abstracts, in octuplicate, should be submitted to the Chairman, Program Committee, 265 Nassau Road, Roosevelt, N. Y.

Grants-in-Aid for Study of Sterility.—The Ortho and Carl G. Hartman grants-in-aid of the American Society for the Study of Sterility, each of $500, are available for 1959. Applications should be sent to the Secretary of the Awards Committee, American Society for the Study of Sterility, Dr. Robert B. Wilson, 200 First St., S. W., Rochester, Minn., by Dec. 31. No application will be considered by the committee unless it is accompanied by five copies of a brief outline of the research project for which the grant-in-aid is being sought.

Anesthesiologists Meeting in Vermont.—The fall meeting of the New England Society of Anesthesiologists will be held at the Equinox Hotel, Manchester, Vermont, Sept. 18-19. Ten papers will be presented under the topics "Old Problems in Anesthesia" and "New Problems in Anesthesia." Speakers include Drs. Richard H. Barrett, Hanover, N. H.; John R. Lincoln, Portland, Maine; Herbert Ebner, Province, R. I.; Morris J. Nicholson, Boston; Emanuel M. Papper, New York City; John Abajian Jr., Burlington, Vt.; Thomas K. Burnap, Boston; James B. Given, Hartford, Conn.; and Robert M. Smith, Boston. Dr. Papper will present two papers. Exhibits are planned, and the social program will include a golf tournament and a banquet. For information write Dr. Thomas K. Burnap, Peter Bent Brigham Hospital, Boston 15.

Nineteen Traveling Science Teachers.—The third Oak Ridge, (Tennessee) Traveling Science Demonstration Lecture Program will take to the road in September and spend the school year visiting high schools in places assigned to them. Each of the 19 specially trained teachers will spend a week at a different high school, giving demonstration lectures and consulting with faculty members on methods of improving science teaching, to interest more students in entering on science and science-teaching careers. Between now and the opening of the next school year, the 19 high school science teachers, who come from eight states and Puerto Rico, will receive intensive training in various fields of science, advanced teaching methods, and classroom and platform techniques. The training will include attendance at a four-week institute for science teachers that will feature lectures and demonstrations by outstanding scientists and educators. The summer training program is under the direction of R. J. Stephenson, Ph.D., professor of physics at the College of Wooster in Ohio.

Meeting on Proctology in Sun Valley.—The Northwest Proctologic Society will meet Aug. 27-29 in Sun Valley, Idaho. Two panel discussions are planned, "Pruritus Ani" and "Problems in Anorectal Surgery," moderated by Drs. William A. McMahon, Seattle, and Curtice Rosser, Dallas, Texas, respectively. The following topics and speakers are scheduled:

Hyperkeratinization of Squamous Epithelial Rests in the Rectal Ampulla, Dr. Walter R. Munroe, Portland, Ore.
Anorectal Applied Anatomy, Drs. Malcolm R. Hill Sr., and Arthur E. Lewis, Seattle.
Recurrent Post Anal Ulcer Following Anorectal Surgery, Dr. Nathan J. Campbell, Portland, Ore.
Construction and Care of Ileostomy. Dr. Julius B. Christensen, Omaha.
Management of Colorectal Adenomata Showing Malignant Changes, Dr. John L. McKay, Seattle.

A forum on "Pre and Postoperative Care and Complications" will be moderated by Dr. Clifford E. Hardwicke, Portland, Ore. The morning of Aug. 30 Dr. Hyrum R. Reichmann, Salt Lake City, will present "Comments on Activity of the American Board of Proctology." For information write Dr. John L. McKay, 645 Medical Dental Building, Seattle 1, Wash.

Annual Meeting on Cerebral Palsy.—The 12th annual meeting of the American Academy for Cerebral Palsy will be held Sept. 25-27 at the Sheraton-Biltmore Hotel, Providence, R. I. The presidential address will be given at the opening general session by Dr. William T. Green, of Boston. An audiovisual section will present the following:

Progressive Muscular Dystrophy, Childhood Type, Functional Evaluation, Dr. Leon Greenspan, New York City.
Handedness, Finger Skills and Speech Laterality, Dr. Temple S. Fay, Philadelphia.
Education and Language Development for the Hard of Hearing, Dr. Raymond M. Rembolt, Iowa City.
Delayed Skeletal Age in Cerebral Palsy and Related Disorders, Drs. Gerald Solomons, Eric Denhoff, and Manuel Horwitz, Providence.

Emotional Changes Following Camp Experience for Two Groups of Handicapped Children, Raymond H. Holden, M.A., Providence.

A closed-circuit T. V. clinic and question-and-answer sessions are planned. A ladies' program is arranged, and entertainment will include a banquet Sept. 25, 8 p. m., and a clambake, Sept. 26. For information write Dr. Raymond R. Rembolt, University Hospital–School, Iowa City, Iowa, Secretary.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	July 26, 1958		July 27, 1957 Total
	Paralytic Type	Total Cases	
New England States			
Maine	..	..	..
New Hampshire	..	..	1
Vermont	..	..	..
Massachusetts	..	..	2
Rhode Island	1	1	..
Connecticut	..	..	1
Middle Atlantic States			
New York	4	6	8
New Jersey	5	10	6
Pennsylvania	4	4	..
East North Central States			
Ohio	2	8	10
Indiana	..	6	5
Illinois	1	3	14
Michigan	4	4	12
Wisconsin	1	1	8
West North Central States			
Minnesota	..	..	8
Iowa	..	..	2
Missouri	..	..	8
North Dakota	..	..	..
South Dakota	..	..	1
Nebraska	..	1	6
Kansas	..	1	2
South Atlantic States			
Delaware	1	1	..
Maryland	..	..	1
District of Columbia	1	1	1
Virginia	4	8	2
West Virginia	4	6	..
North Carolina	2	4	31
South Carolina	1	4	9
Georgia	1	1	..
Florida	1	10	7
East South Central States			
Kentucky	..	1	6
Tennessee	..	..	3
Alabama	..	..	2
Mississippi	..	4	10
West South Central States			
Arkansas	1	2	5
Louisiana	3	5	6
Oklahoma	1	4	9
Texas	16	28	38
Mountain States			
Montana	3	4	..
Idaho	..	1	3
Wyoming	..	..	1
Colorado	1	1	1
New Mexico	..	..	1
Arizona	..	..	2
Utah	1	2	2
Nevada	..	..	..
Pacific States			
Washington	2	2	1
Oregon	..	..	2
California	7	9	28
Territories and Possessions			
Alaska	..	..	..
Hawaii	3	3	..
Puerto Rico	1	1	..
Total	76	147	265

Grants for Research in Parkinson's Disease.—The Parkinson's Disease Foundation has announced that its Research Advisory Board has approved five scientific research grants to institutions and one fellowship out of $150,000 made available for this purpose by the foundation. These grants, the first awarded since the foundation was formed last October, will support projects of scientists in the universities and neurological clinics who will engage specifically in research into the "cause, prevention and cure of palsy." Chairman of the board is Dr. H. Houston Merritt, dean of Columbia University's College of Physicians and Surgeons and director of the Service of Neurology at Presbyterian Medical Center, New York City. Grants to the following were approved: Boston Veterans Administration Hospital, Duke University, Durham, N. C., Iowa State University, Iowa City, Columbia University, and University of Washington, Seattle. The fellowship was awarded to an individual who is to work in the Parkinson Clinic at Massachusetts General Hospital in Boston. Application forms for additional institutional grants, for postgraduate and undergraduate fellowships are now available at the foundation headquarters in the Hotel Beverly in New York City. The Parkinson's Disease Foundation is philanthropically endowed for all its operating expenses, and all donations go directly into scientific research.

Meeting of Mississippi Valley Society in Chicago.—The 23rd annual meeting of the Mississippi Valley Medical Society will be held at the Hotel Morrison, Chicago, Sept. 24-26 under the presidency of Dr. Joseph C. Edwards, of Washington University School of Medicine, St. Louis. Speakers include Dr. Gunnar Gundersen, President, American Medical Association; Dr. Alton Oschner, of Tulane University, New Orleans; Dr. Robert C. Hickey, Iowa State University, Iowa City; and Dr. Mark H. Lepper, University of Illinois, Chicago. There will be six panel discussions; the moderators and the subjects are as follows:

Additional Helpful Procedures for Diagnosis and Prognosis in Jaundice and Liver Disease, Dr. James B. Carey, Mayo Clinic, Rochester, Minn.
Fractures in Children, Dr. John J. Fahey, Chicago.
Pulmonary Diseases, Dr. Paul Murphy, St. Louis University.
Diarrhea in Infancy, Dr. Heyworth N. Sanford, University of Illinois.
Hypertension, Dr. Peter J. Talso, Loyola University.
Menopause, Menorrhagia and Amenorrhea, Dr. Robert B. Wilson, Mayo Clinic.

There will be a scientific and technical exhibit hall, a fellowship hour, and a banquet. All physicians are invited; the program is geared to appeal to those in general practice. The 15th annual meeting of the American Medical Writers' Association will be held in the same hotel on Sept. 26-27. For information write Dr. Harold Swanberg, Secretary, W. C. U. Bldg., Quincy, Ill.

Annual Meeting on Urology.—The Northeastern Section of the American Urological Association will hold its annual meeting Sept. 11-13 at the Equinox House, Manchester, Vermont. The presidential address, "Treatment of Tumors of the Bladder—Past, Present," will be given Sept. 13, 11:45 a. m., by Dr. William A. Milner, Albany. Guest speakers will present the following:

Renal Artery Disease and Hypertension, Dr. Eugene F. Poutasse, Cleveland.
Renal Calculous Disease, Dr. Charles L. Prince, Savannah, Ga.
Chemotherapy in Urological Cancer, Dr. Richard C. Putnam, Philadelphia.
Post-prostatectomy Incontinence, Dr. Victor F. Marshall, New York City.
Hormones and Prostatic Cancer, Dr. William Wallace Scott, Baltimore.
Radiation Biology in Carcinoma of the Bladder, Dr. Marvin N. Lougeed, Montreal, P. Q.

A panel for discussion of the problems in management of advanced cancer is planned for Sept. 13, to be preceded by "Quacks, Charlatans and Urological Cancer," presented by Mr. Oliver A. Field, director of the bureau of investigation, American Medical Association, Chicago. For information write Dr. Francis O. Harbach, 831 James St., Syracuse, N. Y., Secretary-Treasurer.

Society News.—Dr. Daniel E. Jenkins Jr., of Houston, Texas, took office as president of the **American Trudeau Society**, May 23. Other officers include: Dr. Roger S. Mitchell, of Denver, president-elect; Dr. Byron F. Francis, Seattle, vice-president; and Dr. Ejvind P. K. Fenger, Oak Terrace, Minn., secretary-treasurer. Appointed to serve on the executive committee, with the officers, were Dr. Theodore L. Badger, Boston, immediate past-president; Dr. Paul T. Chapman, Detroit; and Dr. Raymond F. Corpe, Rome, Ga.——The following officers of the **American Academy of Tuberculosis Physicians** have been elected: president, Dr. Marcio M. Bueno, New Bedford, Mass.; first vice-president, Dr. Mervin H. Black, Joplin, Mo.; second vice-president, Dr. Zoltan Galambos, Chicago; auditor-editor, Dr. Harry J. Corper, Denver; officer of sessions, Dr. Max Fleishman, Omaha; historian, Dr. Kellie N. Joseph, Birmingham, Ala.; and secretary, Dr. Oscar S. Levin, Denver.——The following officers were elected June 22 at the annual meeting of the **American Diabetes Association**: president, Dr. Alexander Marble, Boston; first vice-president, Dr. Francis D. W. Lukens, Philadelphia; second vice-president, Dr. Franklin B. Peck Sr., Indianapolis; secretary, Dr. Edward P. Sheridan, Denver; and treasurer, Dr. Thomas P. Sharkey, Dayton, Ohio.——The **Society for Investigative Dermatology** has elected the following officers: Dr. Hermann K. B. Pinkus, Monroe, Mich., president, 1958-59; Dr. Thomas B. Fitzpatrick, Portland, Ore., vice-president, 1958-59; Irvin H. Blank, Ph.D., Boston, member, board of directors, 1958-63; Dr. Allan L. Lorincz, Chicago, member, board of directors, 1958-63.

Awards for Contributions in Research.—The Gairdner Charitable Foundation, incorporated in December, 1957, as a charitable corporation under the laws of the Province of Ontario of the Dominion of Canada, has announced the establishment of international awards in two classes: (1) Gairdner Foundation Award of Merit—a prize of $25,000 to be awarded not more than once in every four years to the individual or group who in the opinion of the foundation has made "the most outstanding discovery or contribution in the fields of the arthritic, rheumatic and cardio-vascular diseases"; (2) Gairdner Foundation Annual Awards—a series of prizes of $5,000 each to be awarded in any one year to not more than five individuals who in the opinion of the foundation have made outstanding discoveries or contributions in the same field. All awards will be made at the discretion of the foundation and will not be open to application on the part of potential candidates. Awards may be made to residents of any country and will be payable in Canadian funds. The first awards will be made during 1958. Where traveling expenses are incurred, the amount of the award may be increased. The founder and president of the foundation is Mr. J. A. Gairdner, Canadian financier who provided the initial capital of about $500,000. For information write Mr. Edward Dunlop, General Secretary, Gairdner Charitable Foundation, 320 Bay St., Toronto, Canada.

Research Fellowship for Women Physicians.—The Women's Medical Association of the City of New York offers the Mary Putnam Jacobi Fellowship to a graduate woman physician, American or foreign, to start Oct. 1, 1959, and to amount to $2,000, $1,000 being available Oct. 1, 1959. The recipient will be expected to make a report to the committee at the end of the fourth month, after which the second $1,000 will be awarded subject to the approval of the committee. The fellowship is given for medical research, clinical investigations, or postgraduate study in a special field of medicine. The recipient is expected to devote full time to the fellowship, but exception may be made under special circumstances. Applications must be returned before Feb. 1, 1959, with the following: (1) curriculum vitae, (2) a statement from a physician of a recent physical examination, (3) transcripts of her college and medical school records,

(4) personal letters of recommendation from two or more physicians under whom she has studied, (5) the problems the applicant proposes to investigate or study, (6) a statement from the person under whom she proposes to study of his or her interest in her subject, (7) recent photograph. Successful candidates will be notified not later than May 1, 1959. For information and applications write Dr. Ada Chree Reid, Secretary, The Mary Putnam Jacobi Fellowship Committee, 118 Riverside Drive, New York 24.

Surgeons Celebrate Anniversary of World Federation.—The second anniversary of the formation of World Federations of Surgeons on a continental basis within the structure of the International College of Surgeons will be observed at the Palmer House, Chicago, Sept. 19, when the college will also hold its biennial installation of international officers and officers of the United States and Canadian Sections. The Hon. Benjamin A. Cohen, Ambassador, Under-Secretary, United Nations, New York, will be the principal speaker, covering the role of the medical and surgical profession in cementing international relationships. Dr. Henry W. Meyerding, of Rochester, Minn., will be installed as president of the parent organization, succeeding Prof. Dr. Carlos Gama, of Sao Paulo, Brazil. Dr. Edward L. Compere, of Chicago, will become president of the United States Section, succeeding Dr. Curtice Rosser, of Dallas. Dr. George J. Strean, of McGill University, Montreal, will assume the presidency of the Canadian Section in place of Dr. Richard M. H. Power, of Montreal. Dr. Raymond W. McNealy, of Chicago, will be the banquet chairman, and Dr. Morris Fishbein, of Chicago will be the toastmaster. The federation was launched at the congress of the French Section, International College of Surgeons, at Reims in May, 1957. Four units have been established, covering North America, Central and South America, Europe, and Asia. The active sections in 40 countries form the nuclei of the continental federations comprising 13,000 members. Dr. Rosser is president of the North American Federation, which is composed of the United States, Canada, and Mexico. Information may be had by writing to International College of Surgeons, 1516 Lake Shore Drive, Chicago 10.

Annual Report on Hospitals.—The American Hospital Association has reported that hospitals in the continental United States cared for 22,993,000 patients in 1957, more than in any previous year and an increase of more than 900,000 from the 1956 total of 22,089,000. A total of 3,739,259 babies were born in U. S. hospitals last year, a rise of 248,118 over the 1956 total of 3,491,141 hospital births. On any given day in 1957, an average of 1,320,000 patients and 48,775 newborn infants were hospitalized. Hospital admissions have risen steadily each year since 1946, when the American Hospital Association began its statistical series. The voluntary hospitals which care for the majority of the acute short-term cases in the nation spent an average of $26.81 a day for the care of each patient, an increase of $1.82 over 1956. In these hospitals, the average expenditure on each patient in 1957 was $198.39, compared with $181.43 in 1956. The average patient stay in the voluntary hospitals was 7.4 days (7.5 days in 1956). Total income from patients in all voluntary hospitals in 1957 was $2,878,254,000, while expenses were $3,050,398,000. Patient income made up 94.3% of the total income of all these hospitals in 1957, as compared with 96.1% in 1956. The balance came from contributions, grants, and income from other sources. In 1957, an average of 107 personnel per 100 patients were employed in all hospitals (101 in 1956). More than 260,000 professional nurses worked full-time in hospitals in 1957. Almost 58,000 professional nurses served in hospitals on a part-time basis. More than half of all U. S. hospitals were voluntary; 16% were proprietary; and 32% were operated by agencies of federal, state, or local government. Ninety-five per cent of all hospital admissions last year were to general hospitals. However, psychiatric hospitals cared for 51% of the total number of patients hospitalized on any one day. Thirty-six per cent of all U. S. hospitals had less than 50 beds, 23% had from 50 to 99 beds, 27% had between 100 and 299 beds, and 14% had 300 beds or more.

FOREIGN

Brigidier Boyd Receives Knighthood.—Brigadier J. S. K. Boyd, O. B. E., M.D., president of the Royal Society of Tropical Medicine and Hygiene and a trustee of the Wellcome Trust, was recently honored by Queen Elizabeth II in her Birthday Honours List with a Knighthood "for service to bacteriology." Brigadier Boyd served as director of the Wellcome Laboratories of Tropical Medicine from 1946 until his appointment to the Wellcome Trust in January, 1956. In 1951 he was elected a fellow of the Royal Society for his fundamental work on the classification of the dysentery bacilli and his investigation into bacteriophage.

Congress on Leprology in Tokyo.—The VII International Congress of Leprology, originally scheduled for India, will be held in Tokyo, Japan, Nov. 12-19. The sponsoring organizations are the International Leprosy Association, the Japanese Leprosy Association and the Tofu Kyo-kai (Japanese Leprosy Foundation). Congress headquarters will be the Sankei Kaikan Building and accommodations will be provided for delegates at the Dai-ichi Hotel. Contributors to the program are requested to prepare abstracts of not longer than 200 words and to send two copies to the Secretary, International Leprosy Association, 8 Portman St., London, W. 1, England, and one to the Executive Secretary, Japanese Committee on the VII International Congress of Leprology, ℅ Tofu Kyo-kai, 5 Uchisaiwai-cho, 2-chome, Chiyoda-ku, Tokyo, Japan, by Sept. 1. Complete papers should be sent to the Tokyo address by Sept. 30.

DEATHS IN OTHER COUNTRIES

Lord Webb-Johnson.—A surgeon to Queen Mary, grandmother of the present Queen, for 17 years, Lord Webb-Johnson died in London May 28. The former Alfred Edward Webb-Johnson before his elevation to the peerage as a baronet in 1945, he was created a baron in 1948. He was president of the Royal College of Surgeons for eight years, being awarded its honorary medal in 1950, and received an honorary fellowship in the American College of Gastroenterology the same year.

CORRECTION

Personal.—In the Government Service item entitled "Retirement of Medical Officers" in The Journal, July 26 issue, page 1650, Rear Adm. Joseph W. Kimbrough was erroneously listed as holding the grade of captain and as retiring with more than 32 years active service. He was retired for permanent physical disability.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates, Inc.: The American medical qualification examination to be given henceforth twice a year for foreign medical graduates. Medical Schools in the United States and Foreign Countries, Sept. 23. Final date for filing application was June 23. Dates for the 1959 examinations have been set for Feb. 17 and Sept. 22. Executive Director, Dr. Dean F. Smiley 1710 Orrington Ave., Evanston, Illinois.

BOARDS OF MEDICAL EXAMINERS

Alaska:* On application in Anchorage and Juneau. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

California: *Written Examination.* Sacramento, Oct. 20-23. *Oral Examination.* San Francisco, November 15. *Oral and Clinical Examination for Foreign Medical School Graduates.* San Francisco, November 16. Sec., Dr. Louis E. Jones, 1020 N Street, Sacramento.

Colorado: *Endorsement.* Denver, Oct. 14. *Written.* Denver, Dec. 9-10. Exec. Sec., Mrs. Beulah H. Hudgens, 715 Republic Bldg., Denver 2.

District of Columbia:* *Reciprocity.* Washington, September 8. *Examination.* Washington, Dec. 8-9. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

New Hampshire: *Examination.* Concord, Sept. 10-13. *Reciprocity.* Concord, Sept. 10. Sec., Dr. Mary M. Atchison, Room 101, 61 South Spring St., Concord.

Montana: *Examination and Reciprocity.* Helena, Oct. 7. Sec., Dr. Thomas L. Hawkins, 555 Fuller Ave., Helena.

New Mexico:* *Examination and Reciprocity.* Santa Fe, Nov. 17-18. Sec., Dr. R. C. Derbyshire, 227 East Palace Ave., Santa Fe.

Ohio: *Examination.* Columbus, Dec. 16-18. *Endorsement.* Columbus, August 18; October 6 and Dec. 16-18. Sec., Dr. H. M. Platter, Wyandotte Bldg., Columbus 15.

Oregon:* *Examination.* Portland, Sept. 26-27. Ex. Sec., Mr. Howard I. Bobbitt, 609 Failing Bldg., Portland 4.

Puerto Rico: *Examination.* San Juan, Sept. 2. Sec., Mr. Joaquin Mercado Cruz, Box 9156, Santurce.

Texas:* *Examination and Reciprocity.* Fort Worth, Dec. 4-6. Sec., Dr. M. H. Crabb, 1714 Medical Arts Building, Fort Worth 2.

Wisconsin: *Examination.* Madison, Sept. 19. Sec., Mr. William H. Barber, 621 Ransom St., Ripon.

Wyoming: *Examination and Reciprocity.* Cheyenne, Oct. 6. Sec., Dr. Franklin D. Yoder, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination.* Juneau, Nov. 4. Sec., Dr. R. Harrison Leer, Room 204, Alaska Office Bldg., Juneau.

Arkansas: *Examination.* Little Rock, Oct. 6-7. Sec., Dr. S. C. Dellinger, Zoology Department, University of Arkansas, Fayetteville.

Colorado: *Examination and Reciprocity.* Denver, Sept. 3-4. Sec., Dr. Esther B. Starks, 1459 Ogden St., Denver 18.

District of Columbia: *Reciprocity.* Washington, September 8. *Examination.* Washington, Nov. 13-14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., N. W., Washington 6.

Kansas: *Examination and Reciprocity.* Kansas City, Nov. 24-25. Sec., Dr. L. C. Heckert, Pittsburg.

Michigan: *Exemaination.* Ann Arbor and Detroit, Oct. 10-11. Sec., Mrs. Anne Baker, 116 Stevens T. Mason Bldg., W. Michigan Ave., Lansing 15.

Oklahoma: *Examination and Reciprocity.* Oklahoma City, Sept. 26-27. Sec., Dr. E. F. Lester, 813 Braniff Bldg., Oklahoma City.

Oregon: *Examination.* Portland, Sept. 6. Address: Oregon Basic Science Examining Committee, State Board of Higher Education, Eugene.

Texas: *Examination.* Oct. 13-14. Certificates issued by reciprocity and waiver on the first and fifteenth of each month. Sec., Bro. Raphael Wilson, 407 Perry-Brooks Bldg., Austin.

Wisconsin: *Examination.* Madison, Sept. 19 and Milwaukee, Dec. 6. Sec., Dr. W. H. Barber, 621 Ransom St., Ripon.

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*Basic Science Certificate required.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

Atoms-for-Peace.—The Atomic Energy Commission has made a grant to the Greek Atomic Energy Commission of a nuclear engineering laboratory to be used in the peaceful applications of atomic energy. The grant of about $127,000 is part of a program under Atoms-for-Peace to provide essential equipment for nuclear research and training in friendly nations. The main feature of the laboratory will be a subcritical assembly, including a stainless steel tank, complete lattice assembly, source holder, handling tools, base leveling mechanism, and supporting structures. Fuel for the assembly will consist of 2,500 kg. of canned natural uranium slugs. The fuel transfer to Greece will be arranged under the terms of the existing U. S.-Greek Agreement for Cooperation. The nuclear engineering laboratory will be installed at the new "Democritus" Nuclear Center, near Athens, where the first research reactor in Greece presently is being built. In addition to the subcritical unit, with fuel, the equipment grant includes a 250-mg. radium-beryllium neutron and gamma ray source, neutron and gamma ray counting units, flux mapping equipment, and auxiliary material. The equipment will be used for nuclear research and training. The facilities will be made available to local universities and private industry. Greek authorities have stated that this laboratory will fill a serious gap in their atomic energy program.

A gamma irradiation unit equipped with a cobalt-60 radiation source to be located at the Botanical Institute of the University of Pisa, Italy, has been delivered. The institute will use the gamma source for long term research in the effects of radiation on crops, including improvement of plant breeding processes and discovery of disease-resistant crops, and establish a research center comprising the gamma source, laboratories, greenhouses, and experimental areas. The research center will make its facilities available to agricultural researchers, the Italian Ministry of Agriculture, agricultural experiment stations, and to scientists of other nations. The information developed in the proposed cooperative program will be made available to the United States.

A grant of $36,000 was made to Uruguay for the purchase of nuclear energy equipment. The equipment, comprising a biochemical laboratory, a medical diagnostic laboratory, and a cobalt-60 teletherapy laboratory will be installed at Uruguay's University of the Republic in Montevideo. The university will make available the necessary funds to transport, insure, and maintain the equipment and provide supplementary equipment as necessary. The United States will receive copies of any technical publications resulting from the use of the equipment.

VETERANS ADMINISTRATION

Personal.—Dr. Benjamin B. Wells, director, professional services, VA Hospital, New Orleans, has been appointed to head the VA medical education services in Washington, D. C., succeeding Dr. John C. Nunemaker, who left the VA Aug. 1 to become Associate Secretary of the A. M. A. Council on Medical Education and Hospitals, in Chicago. Dr. Wells, a diplomate of the American Board of Pathology and the American Board of Internal Medicine, received his M.D. degree from Baylor College of Medicine at Dallas and the Ph.D. degree in biochemistry and physiology from the University of Minnesota. He holds the Legion of Merit award and is a lieutenant-colonel in the U. S. Air Force Reserve.——Dr. Ivan F. Bennett, chief of psychiatric research for Veterans Administration in Washington, D. C., has left the VA to work for Eli Lilly & Company in Indianapolis, where he will head clinical research in psychiatry for the company. He also will teach at the University of Indiana School of Medicine and will be a research consultant for the state of Indiana's Division of Mental Health. Dr. Bennett had been with the VA since 1950.

More Hospital Beds for Florida Veterans.—The President has approved the Veterans Administration's request to add 700 more beds through modernization and replacement projects at two of the Florida VA hospitals. On completion of the projects now in the planning stage, 250 beds for the care of mentally ill veterans and 100 beds for general medical and surgical cases will be added at Coral Gables, making a total of 800 beds available there. At present, 450 beds are being operated in the converted Biltmore Hotel which was used as a military hospital during World War II.

At the Bay Pines Hospital near St. Petersburg, plans call for a new 650-bed building and an additional 216-bed treatment section in the old building, which will be modernized.

PUBLIC HEALTH SERVICE

Personal.—Dr. G. Robert Coatney, assistant chief of the Laboratory of Tropical Diseases of the National Institutes of Health received an honorary Doctor of Science degree from Bowling Green State University, Bowling Green, Ohio, on June 8. He has been a consultant on malaria with the National Research Council, the military service, and the World Health Organization. He returned recently from Brazil where he was an advisor on the use of medicated salt as a routine dietary method of administering drugs in the eradication of malaria.

DEATHS

Beers, Daniel Nichols, Pittsfield, Mass.; Yale University School of Medicine, New Haven, 1930; fellow of the American College of Surgeons; specialist certified by the American Board of Surgery; for many years secretary of the Berkshire District Medical Society; associated with Fairview Hospital in Great Barrington, Pittsfield General, Hillcrest, and St. Luke's hospitals; died June 26, aged 52, of tuberculosis and chronic pancreatitis.

Benson, Robert Speer, Avon Park, Fla.; Baylor University College of Medicine, Dallas, Texas, 1905; died May 6, aged 79, of renal failure, and arteriosclerotic heart disease.

Bernstorf, Philip Herman, Wichita, Kan.; Lincoln (Neb.) Medical College of Cotner University, 1905; Northwestern University Medical School, Chicago, 1908; died June 15, aged 76, of arteriosclerotic heart disease.

Bond, Charles Sumner Ⓜ Richmond, Ind.; Bellevue Hospital Medical College, New York City, 1883; served as county coroner and city health officer; member of the Association of American Physicians; past-president of the Union District, Wayne County, and Indiana State Medical societies; for many years assistant surgeon of the Pennsylvania Railroad; served on the board of the Reid Memorial Hospital; died June 16, aged 102.

Bouvier, Charles William, Holyoke, Mass.; University of Vermont College of Medicine, Burlington, 1909; member of the Massachusetts Medical Society; on the staffs of the Holyoke Hospital and the Providence Hospital, where he died June 16, aged 72, of arteriosclerotic cardiovascular disease and diabetes mellitus.

Brandon, John J., Oakland, Calif.; Indiana University School of Medicine, Indianapolis, 1950; interned at Santa Barbara Cottage Hospital in Santa Barbara and San Francisco Hospital; served a residency at the French and the Stanford University hospitals in San Francisco; on the faculty of the Stanford University School of Medicine in San Francisco; veteran of World War II; on the staffs of Peralta, Providence, Merritt, and Highland hospitals; died in Piedmont June 25, aged 41.

Buckles, Joseph H., Waverly, Kan.; Ensworth Medical College, St. Joseph, Mo., 1905; died in Burlington May 11, aged 82, of congestive heart failure.

Buckley, Daniel Joseph, Arlington, Mass.; Tufts College Medical School, Boston, 1904; member of the Massachusetts Medical Society; died in the Symmes Arlington Hospital April 16, aged 78.

Bull, Harry Gifford, Keeseville, N. Y.; Cornell University Medical College, New York City, 1911; died in the Tompkins County Memorial Hospital, Ithaca, June 9, aged 73, of pulmonary embolism.

Burns, M. Q., Blountstown, Fla.; Southern College of Medicine and Surgery, Atlanta, 1913; died in Dothan, Ala., June 15, aged 69, of carcinoma of the prostate.

Canada, Joseph Clayton Ⓜ Tahlequah, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1929; served as health officer at Ada and Tahlequah; service member of the American Medical Association; served as a lieutenant colonel in the U. S. Army Reserve; chief of preventive medicine at Fort Bragg, N. C.; died in the Walter Reed Army Hospital, Washington, D. C., June 14, aged 54, of generalized arteriosclerosis and arteriosclerotic heart disease.

Chalfant, Harry Bailey Ⓜ Kennett Square, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1908; veteran of World War I; formerly on the staff of the Wills Eye Hospital in Philadelphia and the Chester County Hospital at West Chester; died in Wilmington, Del., June 20, aged 75, of cerebral thrombosis and generalized arteriosclerosis.

Champenois, Fern, Hattiesburg, Miss.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; veteran of World War I; associated with the Methodist Hospital; died June 14, aged 74, of a heart attack.

Clark, George Wentworth, Toledo, Ohio; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; veteran of World War I; died June 16, aged 84, of duodenal ulcer with complications.

Cornish, Percy Gillette Ⓜ Albuquerque, N. M.; born in Flagstaff, Ariz., Jan. 10, 1892; Columbia University College of Physicians and Surgeons, New York City, 1918; served as secretary of the New Mexico Board of Medical Examiners; past-president of the Bernalillo County Medical Society; fellow of the American College of Surgeons, of

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Ⓜ Indicates Member of the American Medical Association.

which he was a member of the board of governors; associated with the Bernalillo County–Indian Hospital, St. Joseph Sanatorium and Hospital, Veterans Administration Hospital, and the Presbyterian Hospital Center, where he died June 17, aged 66, of bleeding esophageal varices.

Curtis, Adelaide Harriet Ⓜ Johnstown, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1939; associated with Conemaugh Valley Memorial Hospital, where she died June 21, aged 48, of cerebral hemorrhage.

Deming, Herbert Van Vechten, Cumberland, Md.; Atlantic Medical College, Baltimore, 1907; member of the Medical and Chirurgical Faculty of Maryland; served as secretary of the Allegany County Medical Society; deputy medical examiner of Allegany County; on the staffs of the Sacred Heart Hospital and the Memorial Hospital; died in the Broaddus Hospital, Philippi, W. Va., May 9, aged 78, of cancer of the pharynx with massive hemorrhage.

Devereux, James Marks, Cherryvale, Kan.; Northwestern University Medical School, Chicago, 1923; member of the Industrial Medical Association; formerly medical director of the Kansas Ordnance Plant at Parsons; veteran of World War II; died in Wichita June 13, aged 58, of coronary occlusion.

Dunn, Romantes Henry, Azusa, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1921; on the staff of the Alta District Hospital in Dinuba; died June 13, aged 71, of arteriosclerosis.

Dunton, Allen Henry, Cincinnati; University of Michigan Homeopathic Medical School, Ann Arbor, 1911; Eclectic Medical College, Cincinnati, 1915; veteran of World War I; died in the Veterans Administration Hospital June 21, aged 70, of myocardial infarction and arteriosclerosis.

Ellis, Alexander Ⓜ Collingswood, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1920; plunged to his death from his seventh floor apartment June 19, aged 62.

Emery, George Edwin Ⓜ Boylston Center, Mass.; Harvard Medical School, Boston, 1897; veteran of World War I; for many years practiced in Worcester, where he was physician for the public schools, and on the staffs of the Fairlawn, Memorial, and Belmont hospitals, and the Worcester City Hospital, where he died June 18, aged 88.

Epstein, Samuel Gerald Ⓜ Detroit; Detroit College of Medicine and Surgery, 1933; member of the American Society of Anesthesiologists; fellow of the International College of Surgeons; served during World War II; died June 12, aged 49.

Gates, George Francis Ⓜ Chicago; Bennett Medical College, Chicago, 1913; member of the American Academy of General Practice; died April 1, aged 72, of coronary occlusion.

Gordon, Paul Metz Ⓜ Bay Village, Ohio; Western Reserve University School of Medicine, Cleveland, 1927; associated with St. John's, Fairview, and Lutheran hospitals in Cleveland, and Lakewood (Ohio) Hospital, where he died June 17, aged 55, of cancer of the mouth.

Hall, Fairfax Ⓜ Christiansted, Virgin Islands; Columbia University College of Physicians and Surgeons, New York City, 1911; member of the Medical Society of the State of New York; formerly practiced in New Rochelle, N. Y., where he was on the staff of the New Rochelle Hospital; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; died June 4, aged 72, of coronary disease.

Hamborszky, Eugene Julius, Millheim, Pa.; Medico-Chirurgical College of Philadelphia, 1912; died in Williamsport, Md., May 20, aged 71, of portal cirrhosis.

Hamilton, Grover Cleveland Ⓜ Piedmont, Ala.; born in Coal City, Ala., Oct. 23, 1888; Medical Department of Emory University, Atlanta, 1916; veteran of World War I; for many years city health officer; served on the city school board; surgeon for the Seaboard Air Line Railroad; member of the American Association of Railroad Surgeons and the Southern Medical Association; associated with the Piedmont Hospital, where he was a member of the board; in 1954 named Piedmont's "Man of the Year," the first time the Chamber of Commerce created this post; died in the Georgia Baptist Hospital, Atlanta, June 17, aged 69, of a head injury as the result of an automobile accident.

Hand, William Robert Ⓜ Philadelphia, Miss.; Memphis (Tenn.) Hospital Medical College, 1909; died June 5, aged 78.

Hantman, Harold Ⓜ Newark, N. J.; University and Bellevue Hospital Medical College, New York City, 1931; fellow of the American College of Surgeons; on the staffs of the Presbyterian Hospital, Martland Medical Center, and Clara Maass Hospital; died June 8, aged 50.

Harris, Dallie Patterson, Union City, Tenn.; Meharry Medical College, Nashville, 1931; on the staff of the Obion County General Hospital, where he died May 12, aged 59, of acute myocardial decompensation.

Hartsuck, David Schively Ⓜ Seattle; University of Oregon Medical School, Portland, 1943; veteran of World War II; on the staff of the Swedish Hospital; died June 16, aged 42.

Harwich, Moses, New York City; Columbia University College of Physicians and Surgeons, New York City, 1905; an associate member of the American Medical Association; served on the staff of the Lebanon Hospital; died May 14, aged 74, of coronary occlusion.

Hayes, William Van Valzah, New York City; born in 1867; Columbia University College of Physicians and Surgeons, New York City, 1893; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; member of the House of Delegates of the American Medical Association in 1918-1919; served on the faculty of the New York Polyclinic Medical School and Hospital; associated with St. John's Riverside Hospital in Yonkers, and Polyclinic and New York hospitals in New York City; died in Greenwich, Conn., June 27, aged 90, of congestive heart failure.

Heald, Clarence Linden Ⓜ Sigourney, Iowa; University of Pennsylvania Department of Medicine, Philadelphia, 1893; fellow of the American College of Surgeons; died May 25, aged 90.

Heard, Thomas Marsden Jr., Palatka, Fla.; University of Buffalo School of Medicine, 1899; veteran of World War I; died April 17, aged 86, of ruptured abdominal aneurysm.

Hillman, Rolfe Louis Ⓜ Emory, Va.; Johns Hopkins University School of Medicine, Baltimore, 1918; member of the American Academy of General Practice; physician at Emory and Henry College; died in Nashville, Tenn., June 23, aged 67.

Holeman, Charles Joseph Ⓜ Medical Director, Captain, U.S.N., retired, Arlington, Va.; born in Philadelphia March 14, 1880; University of Pennsylvania Department of Medicine, Philadelphia, 1907; commissioned in the medical corps of the U. S. Navy as a lieutenant (jg) in September, 1907, and served for more than 36 years on active duty until his retirement in April, 1944; advancing progressively through the commissioned ranks of the Navy, attained the rank of captain in July, 1929; during his naval career, served with the medical department of the Navy throughout the United States and abroad, and in ships of the fleet; duty stations and assignments from 1935 until his retirement were at the Bureau of Medicine and Surgery, Washington, D. C., where he was assigned to the planning division, the U. S. Naval Hospital, Pearl Harbor, T. H., as commanding officer, the U. S. Naval Hospital, Mare Island, Calif., as commanding officer, and on the staff of the commandant, 13th Naval District, Seattle, as district medical officer; two years after his retirement from the Navy, was employed by the Veterans Administration as secretary of special boards and continued in that capacity until May, 1950, when he again retired; service member of the American Medical Association; died in the U. S. Naval Hospital, Bethesda, Md., June 21, aged 78.

Huffines, Thomas Ruffin Ⓜ Asheville, N. C.; born in Rocky Mount, Jan. 10, 1894; Indiana University School of Medicine, Indianapolis, 1919; specialist certified by the American Board of Urology; member of the Southeastern Surgical Congress and the American Urological Association; fellow of the American College of Surgeons; veteran of World War I; associated with the Western North Carolina Tuberculosis Sanitarium in Black Mountain, Ashton Park (N. C.) Hospital, and St. Joseph's and Memorial Mission hospitals; consultant at the Veterans Administration Hospital in Swannanoa; died May 25, aged 64, of congestive heart disease.

Hulka, Jaroslav H., Long Island City, N. Y.; Universita Karlova Fakulta Lékarská, Praha, Czechoslovakia, 1919; member of the Medical Society of the State of New York and the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; certified by the National Board of Medical Examiners; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; on the staff of the Manhattan Eye and Ear Hospital in New York City and St. John's Long Island City Hospital; died in the Harkness Pavilion, Columbia-Presbyterian Medical Center, New York City, June 18, aged 64.

Huyck, Stanhope Pier, Sunfield, Mich.; University of Michigan Medical School, Ann Arbor, 1927; veteran of World War II; served on the staff of St. Lawrence Hospital in Lansing; died in Detroit May 14, aged 54.

Iskot, Herman, Long Island City, N. Y.; Friedrich–Wilhelms–Universität Medizinische Fakultät, Berlin, Prussia, Germany, 1926; died June 24, aged 69, of coronary thrombosis.

Jarvis, James Raymond Ⓜ Van Wert, Ohio; George Washington University School of Medicine, Washington, D. C., 1931; member of the American Society of Anesthesiologists and the American Academy of General Practice; served as president of the Ohio Academy of General Practice; died in the Cleveland Clinic Hospital June 27, aged 52, of multiple brain abscess.

Jones, Cody Harrison, Lynn Grove, Ky.; University of Louisville School of Medicine, 1912; died May 20, aged 74, of coronary occlusion.

Kalal, Elmer John Ⓜ Sheridan, Ill.; University of Illinois College of Medicine, Chicago, 1937; member of the American Academy of General Practice; on the staff of the Horatio N. Woodward Memorial Hospital in Sandwich; director of the Sheridan State Bank; died in Serena May 19, aged 56, of cancer.

Keen, Frank Martin Ⓜ Shawnee, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1932; fellow of the American College of Surgeons; past-president of the Pottawatomie County Medical Society; on the staff of the Shawnee City Hospital; died May 16, aged 54, of coronary disease.

Keichline, John Maulfair, Middleburg, Pa.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1902; an associate member of the American Medical Association; specialist certified by the American Board of Radiology; veteran of the Spanish-American War and World War I; at one time a medical missionary in Cairo, Egypt; served as county coroner and as secretary-treasurer of the American Registry of X-Ray Technicians; for many years practiced in Huntington, where he was radiologist at J. C. Blair Memorial Hospital; died in the Lewisburg (Pa.) Hospital June 10, aged 80, of arteriosclerosis.

Keim, Cameron Dolson Ⓜ Lansing, Mich.; University of Michigan Medical School, Ann Arbor, 1927; on the staff of the Olin Memorial Health Center of Michigan State University; died May 26, aged 61.

Kennedy, George Russell Ⓜ Camden, N. J.; Northwestern University Medical School, Chicago, 1928; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; veteran of World War II; served on the faculty of Jefferson Medical College of Philadelphia; on the staff of the West Jersey Hospital; died May 15, aged 57, of massive coronary occlusion.

Kerr, William John Jr. Ⓜ San Rafael, Calif.; Harvard Medical School, Boston, 1944; interned at Peter Bent Brigham Hospital in Boston; served a residency at the University of California Hospital and Children's Hospital in San Francisco; specialist certified by the American Board of Pediatrics; on the staffs of the Children's Hospital in San Francisco, Ross (Calif.) Hospital, and the San Rafael General Hospital; died May 26, aged 39, after swallowing an insecticide, self-administered.

Key, Sothoron Ⓜ Washington, D. C.; Columbia University Medical Department, Washington, 1899; veteran of World War I; died May 28, aged 85.

King, Cecil Valentine, Los Angeles; Northwestern University Medical School, Chicago, 1924; formerly on the staff of the Gallinger Municipal Hospital in Washington, D. C.; died in the Good Samaritan Hospital June 2, aged 61, of carcinoma of the prostate.

King, Oliver Doyle Ⓜ Bremen, Ga.; Emory University School of Medicine, Atlanta, 1926; died May 8, aged 60, of an accidental gunshot wound.

Kingman, Lucius Collinwood Ⓜ Providence, R. I.; born in Providence July 29, 1878; Harvard Medical School, Boston, 1904; member of the founders group of the American Board of Surgery; member of the American Urological Association; fellow of the American College of Surgeons; past-president of the Rhode Island Medical Society and the New England Surgical Association; served overseas with the British Army and U. S. Navy during World War I; a member of the board of hospital commissioners of Providence; consultant, Rhode Island, Charles V. Chapin, Butler, Veterans Administration, and Providence Lying-in hospitals in Providence, Memorial Hospital in Pawtucket, and Westerly (R. I.) Hospital; died in the Jane Brown Hospital June 19, aged 79.

Kinley, Thomas Fulton Ⓜ Rockford, Ill.; Chicago College of Medicine and Surgery, 1908; served on the staff of St. Anthony Hospital; died June 6, aged 86, of terminal pneumonia.

Kirkland, Thomas Andrew Ⓜ Memphis, Tenn.; Mississippi Medical College, Meridian, 1908; died June 11, aged 76, of cerebral vascular accident, and arteriosclerosis.

Koch, Robert Frederick Ⓜ Hallis, N. Y.; Long Island College Hospital, Brooklyn, 1908; on the staff of the Wyckoff Heights Hospital, in Brooklyn, where he died June 14, aged 72, of acute pulmonary edema due to arteriosclerotic heart disease.

Kolvoord, Theodore Ⓜ Battle Creek, Mich.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1912; specialist certified by the American Board of Radiology; veteran of World War I; died in the Community Hospital June 7, aged 69, of cerebral thrombosis.

Krueger, Frederick William Ⓜ Richmond, Ind.; Miami Medical College, Cincinnati, 1903; on the staff of the Reid Memorial Hospital, where he died June 15, aged 79, of acute myocardial infarction, arteriosclerotic heart disease, and hemiplegia.

Kuhlman, Mosheim W., Johnstown, Pa.; College of Physicians and Surgeons, Baltimore, 1912; past-president of the medical staff of Conemaugh Valley Memorial Hospital; died May 12, aged 73.

Lankford, Anthony Ernest, Stephenville, Texas; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1898; veteran of World War I; served as city and county health officer; died June 8, aged 80, of myocardial infarction.

Larsen, Myron Wilbur Ⓜ Watertown, S. D.; Rush Medical College, Chicago, 1926; member of the American Academy of General Practice; died in Sioux Falls May 7, aged 61.

Lauderdale, Clay, Austin, Texas; University of Tennessee College of Medicine, Memphis, 1907; served as director of the Austin State School; died June 23, aged 73.

Lawrence, Frank Heistand, Reading, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1906; an associate member of the American Medical Association; served on the staff of St. Joseph's Hospital; died June 11, aged 74.

Leavenworth, Loyal Eldredge Ⓜ Canton, Ohio; Western Reserve University School of Medicine, Cleveland, 1914; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; past-president of the Stark County Medical Society; one of the organizers and first president of the Canton Art Institute; veteran of World War I; on the staffs of the Aultman Hospital and the Mercy Hospital, where he died May 20, aged 69.

Leighton, Lewis Lancaster Ⓜ Fort Dodge, Iowa; State University of Iowa College of Medicine, Iowa City, 1922; member of the American Academy of General Practice; past-president of the Webster County Medical Society; veteran of World War I; on the staffs of the Lutheran Hospital and St. Joseph Mercy Hospital, where he died June 10, aged 65, of cancer of the bronchus.

Lewis, Robert Morton Ⓜ New Haven, Conn.; University of Pennsylvania Department of Medicine, Philadelphia, 1910; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; formerly associate clinical professor of obstetrics and gynecology at Yale University School of Medicine; veteran of World War I; on the staff of the New Haven Hospital; died June 20, aged 72, of acute coronary thrombosis.

Luntz, Joseph, Lake Ronkonkoma, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1921; member of the Medical Society of the State of New York; interned at the Lebanon Hospital in New York City; died in the Manhattan Memorial Hospital, New York City, April 28, aged 58, of intestinal cancer with metastases.

Lyons, Edward James Ⓜ Buffalo; University of Buffalo School of Medicine, 1919; veteran of World War I; Canisius College in 1934 awarded him its first La Salle Medal, given annually to its outstanding alumnus; associated with the Sisters of Charity Hospital; died June 12, aged 65.

Mabon, Thomas McCance Ⓜ Pittsburgh; Harvard Medical School, Boston, 1917; professor of preventive medicine at the University of Pittsburgh School of Medicine; specialist certified by the American Board of Internal Medicine; member of the American Psychosomatic Society; fellow of the American College of Physicians; past-president of the Allegheny County Medical Society; on the staff of the Presbyterian Hospital, where he died June 12, aged 67, of cancer of the right lung with metastasis.

MacDonald, John Alexander Ⓜ Interlaken, N. Y.; Rush Medical College, Chicago, 1901; formerly professor of medicine at the Indiana University School of Medicine, Indianapolis; member of the Central Society for Clinical Research, of which he was a founder; fellow of the American College of Physicians; past-president of the Marion County (Ind.) Medical Society; veteran of World War I; served on the staffs of the Indianapolis City, Methodist Episcopal, and Indiana University hospitals, all in Indianapolis; died June 17, aged 81, of dissecting aneurysm of the abdominal aorta.

McCaffrey, Charles Francis Jr., Commander, U. S. Navy, retired, Arlington, Va.; born in Somerville, Mass., Oct. 19, 1906; Georgetown University School of Medicine, Washington, D. C., 1933; an associate member of the American Medical Association; appointed an assistant surgeon with the rank of lieutenant (jg) in the U. S. Naval Reserve in February, 1937, and in August, 1937, transferred to the regular Navy; advanced to the rank of commander in July, 1945, and was placed on the retired list of the Navy on Feb. 1, 1951, by reasons of physical disability; designated a flight surgeon on Sept. 29, 1939, spent most of his 13 years active duty assigned to Naval Air Stations ashore and aircraft carriers at sea; during World War II served aboard the USS Wasp and the USS Yorktown; awarded the Presidential Unit citation for service aboard the Yorktown; prior to his retirement was serving at the Marine Corps Air Station, Cherry Point, N. C.; assistant public health director in Arlington; died in the Arlington Hospital June 25, aged 51.

Mead, John William Ⓜ Poughkeepsie, N. Y.; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1935; member of the Industrial Medical Association; veteran of World War II; on the staffs of St. Francis Hospital and the Vassar Brothers Hospital, where he died June 6, aged 54.

Meisner, Adolph, Brooklyn; Eclectic Medical College, Cincinnati, 1928; veteran of World War II; on the staff of the Unity Hospital; died in the Van Etten Hospital, New York City, June 27, aged 58, of cancer.

Mendez, Luis, New York City; Universidad Nacional Facultad de Medicina, Bogotá, Columbia, 1921; member of the Medical Society of the State of New York; associated with the New York Polyclinic Hospital, where he died May 1, aged 62, of generalized carcinomatosis and adenocarcinoma of the colon.

Nail, William R. Ⓜ Waco, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1890; died June 4, aged 97.

Nesbitt, Clarence Clark, Palmyra, N. Y.; University of Buffalo School of Medicine, 1910; an associate member of the American Medical Association; member of the Industrial Medical Association; served as health officer and president of the village; associated with the Sisters of Charity Hospital in Buffalo; veteran of World War I; at one time practiced in Holley, during which time he served as an Orleans County coroner; died June 6, aged 74, of cancer of the lung.

Nicholas, Constantine Z. Ⓜ La Jolla, Calif.; University of Moscow Faculty of Medicine, Russia, 1916; specialist certified by the American Board of Obstetrics and Gynecology; associated with the Mercy Hospital in San Diego and the Scripps Memorial Hospital in La Jolla; died June 12, aged 66, of a heart attack.

Nielsen, Alvin Martin Ⓜ Northfield, Minn.; University of Minnesota Medical School, Minneapolis, 1940; member of the American Academy of General Practice; veteran of World War II and was decorated with the Navy merit award and Purple Heart; on the staff of the Northfield City Hospital; died June 23, aged 49, of coronary disease.

Olcott, George Potts Jr., East Orange, N. J.; New York Homeopathic Medical College and Flower Hospital in New York City, 1909; veteran of World War I; served as assistant medical examiner of Essex County; at one time pathologist at Orange (N. J.) Memorial Hospital; died in Vineland June 16, aged 75, of cerebral hemorrhage.

Parker, Sheppie Rufus Ⓜ Aliceville, Ala.; University of Alabama School of Medicine, Mobile, 1909; died June 25, aged 75, of coronary thrombosis.

Parry, Glendon E. Ⓜ Hillsboro, Ohio; University of Cincinnati College of Medicine, 1951; member of the American Academy of General Practice; interned at the Christ Hospital in Cincinnati; aged 35; killed when his sports car skidded June 18.

Pettet, Joseph David Ⓜ Pittsburgh, Kan.; St. Louis College of Physicians and Surgeons, 1900; veteran of World I; on the staff of the Mount Carmel Hospital, where he died May 25, aged 83, of coronary thrombosis.

Platou, Erling Stoud Ⓜ Minneapolis; born in Cooperstown, N. D., Aug. 30, 1896; University of Minnesota Medical School, Minneapolis, 1921; clinical professor of pediatrics at his alma mater and the University of Minnesota Graduate School; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; past-president of the Minnesota State Board of Health and the University of Minnesota Alumni Association; for many years president of the Minnesota Medical Foundation; associated with Northwestern Hospital, where he was president of the staff, Abbott, and University of Minnesota hospitals; died in Grand Marais, Minn., June 17, aged 61, of coronary sclerosis.

Ransohoff, Joseph Louis Ⓜ Cincinnati; Medical College of Ohio, Cincinnati, 1904; professor emeritus of clinical surgery at the University of Cincinnati College of Medicine; member of the Western Surgical Association; fellow of the American College of Surgeons; veteran of World War I; specialist certified by the American Board of Surgery; on the staff of Cincinnati General Hospital; director of surgery, Jewish Hospital, where he died June 17, aged 78, of perforated duodenal ulcer.

Rasmussen, Waldemar Curtis Ⓜ Colorado Springs, Colo.; born in Provo, Utah, Feb. 5, 1912; University of Minnesota Medical School, Minneapolis, 1936; specialist certified by the American Board of Psychiatry and Neurology; member of the American Academy of Neurology and the Central Neuropsychiatric Association; interned at Philadelphia General Hospital in Philadelphia; later a resident physician in the University of Florida Infirmary, Gainesville, Fla.; in 1938 became a fellow in medicine at the Mayo Foundation in Rochester, Minn., and in October, 1941, was appointed a first assistant in neurology; in July, 1942, appointed to the staff of the Mayo Clinic in Rochester, Minn., as a consultant in neurology; later became consultant in neurology at the Colorado Springs Medical Center; veteran of World War II; died June 10, aged 46, as the result of an automobile accident.

Ritter, William Joseph, Philadelphia; Medico-Chirurgical College of Philadelphia, 1902; also a graduate in pharmacy; served on the faculty of his alma mater; died June 19, aged 82, of arteriosclerotic heart disease.

Roberts, Mortimer E. Ⓜ Grand Rapids, Mich.; Detroit College of Medicine, 1889; member of the staff of the Blodgett Memorial Hospital, where he died June 9, aged 89, of biliary tract obstruction and renal and cardiac failure.

Robinson, William T. Ⓜ New York City; Boston University School of Medicine, 1920; member of the Industrial Medical Association and the Radiological Society of North America; on the staff of the Bellevue Hospital; served on the staff of the Harlem Hospital; died in the Doctors Hospital June 19, aged 65.

Russell, Guy Jewell, Siloam, Kan.; University of Kansas School of Medicine, Kansas City, Kan., 1906; died in the Trinity Lutheran Hospital, Kansas City, Mo., May 31, aged 77, of acute coronary thrombosis.

Sawyer, Olin, Georgetown, S. C.; Medical College of South Carolina, Charleston, 1901; served as mayor of Georgetown, chairman of the city board of health, and state senator; died in the Georgetown County Memorial Hospital June 6, aged 83, of cerebral thrombosis.

Scheetz, Herbert Nicholas, Allentown, Pa.; Jefferson Medical College of Philadelphia, 1905; an associate member of the American Medical Association; died April 14, aged 75, of arteriosclerotic heart disease.

Schmidt, Frederick Sextus Ⓜ Boston; Harvard Medical School, Boston, 1899; also a graduate in pharmacy; died March 26, aged 85, of coronary thrombosis and arteriosclerosis.

Secor, Charles Edgar Ⓜ Elko, Nevada; Wisconsin College of Physicians and Surgeons, Milwaukee, 1905; past-president of the Nevada State Medical Association; served in France during World War I; on the staff of the Elko General Hospital, where he died June 2, aged 76, of cerebral hemorrhage.

Stanley-Brown, Margaret Ⓜ Washington, Conn.; Columbia University College of Physicians and Surgeons, New York City, 1923; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; formerly practiced in New York City, where she was on the faculty of the New York Medical College, Flower and Fifth Avenue Hospitals, and on the courtesy staffs of the Doctors and City hospitals; surgeon on the attending staff of the New Milford (Conn.) Hospital, where she died June 12, aged 62, of cancer of the sigmoid.

Strickland, Williard Milo, Wendell, N. C.; Medical College of Virginia, Richmond, 1919; died in the Mary Elizabeth Hospital in Raleigh June 3, aged 65, of uremia and chronic pyelonephritis.

Suggett, Orril Le Grand, Lexington, Ky.; Barnes Medical College, St. Louis, 1893; served on the faculty of his alma mater; veteran of World War I; died June 3, aged 85, of arteriosclerotic heart disease.

Tamisiea, John Alexander Ⓜ Omaha; born in Missouri Valley, Iowa, May 13, 1893; John A. Creighton Medical College, Omaha, 1916; specialist certified by the American Board of Preventive Medicine; member of the Aero Medical Association, of which he was past-president; past-president and a charter member of the Civil Aeronautical Medical Association; first vice-president of the Air Line Medical Examiners Association; for many years a flight surgeon and medical examiner for the U. S. Department of Commerce and for United Air Lines; veteran of World Wars I and II and the Korean War; member of the staff and board of directors of the Doctors Hospital; on the staffs of the Children's Memorial, St. Catherine's, and St. Joseph's hospitals; died June 5, aged 65, of congestive heart disease.

Tomec, Otto Carl Frederick Ⓜ Trenton, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1933; interned at the New York Homeopathic Medical College and Flower Hospital, New York City, where he served a residency; veteran of World War II; associated with the McKinley Memorial Hospital; died in Yardley, Pa., June 14, aged 49, of carcinomatosis.

Trentzsch, Philip John, Borrego Springs, Calif.; Vanderbilt University School of Medicine, Nashville, Tenn., 1917; specialist certified by the American Board of Psychiatry and Neurology; member of the American Psychiatric Association and the Medical Society of the State of New York; served on the staff of St. Elizabeth's Hospital in Washington, D. C.; for many years practiced in New York City; died in the Pioneers Memorial Hospital, Brawley, June 11, aged 69, of coronary thrombosis.

Tuttle, Floyd Wilkins Ⓜ Clinton, Iowa; University of Missouri School of Medicine, Columbia, 1909; member of the Missouri State Medical Association; died in Mount Pleasant March 11, aged 81, of pneumonia.

Van Benschoten, George W. Ⓜ Kingston, R. I.; Northwestern University Medical School, Chicago, 1896; fellow of the American College of Surgeons; past-president of the Providence Medical Society; veteran of World War I; served on the staffs of the Rhode Island Hospital, St. Joseph's Hospital, Miriam Hospital, and Roger Williams Hospital in Providence, where he practiced for many years, and South County Hospital in Wakefield; died June 1, aged 81.

Vinson, John Clifford Ⓜ Fort Myers, Fla.; Atlanta (Ga.) School of Medicine, 1906; past-president of the Florida Medical Association; died June 10, aged 74.

FOREIGN LETTERS

AUSTRIA

Obstetric Hemorrhages.—At the meeting of the Society of Physicians in Vienna on June 20, Dr. P. Elsner said that genital bleeding during pregnancy and parturition presents a serious problem. Most of these hemorrhages are due to mechanical factors. Certain severe uncontrollable hemorrhages, although infrequent, are, however, due to true disturbances of blood coagulation based on a deficiency of fibrinogen, and they are designated obstetric hemorrhagic diathesis. They occur chiefly in association with other obstetrical complications, such as ablatio placentae, missed labor, amniotic fluid embolism, and toxicosis. Defibrination may result from intravascular activation of the coagulation system or the activation of the fibrinolytic system. The diagnosis of obstetric hemorrhage is made by means of Scott's test, by determining fibrinogen by the rapid method of Schulz, and by Hartert's test for clot elasticity. Treatment consists of complete emptying of the uterus, administration of fibrinogen, restoration of blood volume, and control of shock.

Anemia During Pregnancy.—At the same meeting Dr. Braitenberg said that iron deficiency was the cause of more than 90% of the cases of anemia in pregnant women. This anemia is of the hypochromic type with a low color index, and it is diagnosed by means of the determination of the iron content of the serum and by the total iron-combining power. Since iron is absorbed in only small quantities, iron metabolism can be seriously impaired by menstrual bleeding. A large physiological iron loss is caused by pregnancy and parturition. The entire iron reserve (2 Gm.) can be depleted after two pregnancies. Of 57 pregnant women, 38 showed a high degree of iron deficiency. The determination of the iron content and of the total protein-combining power leads to the detection of those forms of iron deficiency in which the blood findings are still normal. After an injection of 1 Gm. of iron intravenously the findings returned to normal, the general condition of the patients improved, and they recovered far more rapidly after parturition. Far less frequent are the aplastic anemias of the pernicious type which result from deficient absorption or an increased breakdown of vitamin B_{12} and which subside after the administration of vitamin B_{12}.

Treatment of Toxicosis.—At the same meeting Dr. F. Brandstetter stated that the earlier heroic therapeutic measures in patients with eclampsia have been abandoned in favor of conservative treatment. The lytic cocktail was given as an emergency measure to patients with frank eclampsia. This reduced the case fatality rate from about 18% to about 1% but did not reduce the infant death rate. From the preventive standpoint strict supervision of the pregnant woman is important, as it may help to detect the disease in its incipiency and reduce the infant mortality to a minimum.

Functional Genital Hemorrhages.—At the same meeting Dr. E. Gitsch recommended the two-hormone treatment (10 mg. of estradiol monobenzoate and 250 mg. of a long-acting progesterone) in addition to chorionic gonadotropin to control bleeding in young women and in patients with juvenile metrorrhagia, whereas in the menopause androgens should be used after carcinoma is ruled out. Experience with 19-nor-testosterone showed promising results in patients with functional bleeding, but the experience was not extensive enough to permit a definite conclusion. The two-hormone treatment should be restricted largely to younger women and it should not be given to patients who have reached the menopause inasmuch as the treatment with estrogens and corpus luteum hormone provides the patients with those hormones which should disappear during the menopause. The result is stimulation of the endometrium and repeated bleeding. The more often this two-hormone treatment is repeated the longer are the intervals between the biopsy examinations of the endometrium likely to be. One is confronted with the problem of whether to repeat the curettage or to overlook an incipient carcinoma. The speaker preferred steroids during the menopause which cause no proliferation of the endometrium or other adverse effects on the gonads.

Chromosomal Sex Differentiation.—At the same meeting Dr. E. Schueller said that chromosomal sex differentiation was an essential routine examination in gynecology, particularly in determining the genesis of a primary amenorrhea, as well as in pediatrics and urology in patients who showed certain symptoms. It is, therefore, practical to select from the existing modifications that method of determination in which the optimal demonstration of the chromosomal sex characteristics is technically easy to perform. Sex cannot be determined re-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

liably by means of the sex chromatin nuclear attachment of the polynuclear leukocytes in the blood smear. Not only is the examination of 500 leukocytes difficult but also the morphologic differentiation is not characteristic enough. Examination of exfoliated cells from the buccal mucosa is preferred. The so-called sex chromatin body of the cells of genetically female persons is demonstrable not only by means of the Fuelgen reaction but also after hydrochloric acid hydrolysis at room temperature and after staining of the nuclear chromatin with buffered thionine solution. The sex chromatin can also be demonstrated clearly in histological sections in the manner described, but in patients with malignant tumors the demonstration of sex chromatins is difficult even if one's technique is perfect, because of the clubbing of the nuclear chromatins of the tumor cells, which often show polyploid chromosomal substance. The staining method with cresyl violet, which is frequently used, does not demonstrate the sex chromatin clearly enough.

BRAZIL

The Skeleton in Malignant Hemopathies.—The radiologic study of the skeleton is important in the malignant hemopathies, not only due to the high frequency of the bone lesions but also because of the diagnostic help it can give in some patients, according to Dr. Rafael Barros and co-workers of the Hospital das Clinicas in São Paulo. They studied 100 patients with malignant hemopathies (24 with acute and 22 with chronic granulocytic leukemia, 19 with malignant lymphogranulomatosis, 19 with reticulosarcoma and lymphosarcoma, 5 with multiple plasmocytic myeloma, 5 with carcinomatosis, and 3 with acute and 3 with chronic lymphocytic leukemia). No relationship was seen between the severity of the bone lesions and the duration of the disease. The most frequent types of lesion, not pathognomonic of any of the hemopathies studied, in order of importance, were longitudinal lines of diaphysial rarefaction; condensing osteitis of the lower extremity; osteolytic foci in the skull, hands, and limbs; transverse bands of metaphysial rarefaction; periosteal reaction; areas of condensation alternating with zones of rarefaction in the skull; condensing osteitis of the margins of the orbit; development of "Mephistophelean features"; and increased pneumatization of the accessory cavities of the nose.

Ascariasis of Biliary Ducts.—Dr. Roldão Consoni (*Revista da Associação medica brasileira*, vol. 4, [March] 1958) reported a series of four patients with ascariasis of the biliary ducts, all of whom were operated on. In two patients there was an ascaris in the common bile duct, and each of the other two had three in the common bile duct and three in the intrahepatic bile ducts. Dr. Consoni calls attention to an easy means of removing ascaris from the deep bile ducts—the use of a malleable suction cannula. Anthelminthics must be given postoperatively across the T tube in the common duct as soon as the patient's condition permits. The tube should be removed only when the test for ascaris ova in the bile becomes negative.

Dermopathies from Intestinal Parasites.—Dr. Orlando Henrique França (*Pediatria prática*, vol. 39, 1958) calls attention to the fact that there are two theories to explain the genesis of the skin disturbances associated with intestinal parasitism. One is based on allergy and the other on the effect of the toxic products of the parasites. Amebiasis causes a general intoxication as shown by itching skin lesions. Three hypotheses have been advanced to explain the pathogenesis of amebic disturbances outside of the intestines: (1) metastasis or invasion of the blood by the parasite, causing a general intoxication (allergic toxemia); (2) blood parasitism, or the ability of the parasite to establish a secondary habitat in the blood, whence it migrates to any region of the body and causes various lesions; and (3) sensitization of the tissues with the participation of bacteria from the intestines and other products of enteric origin. The hypochromic spots seen on the skin are the result of an intoxication caused by Ascaris lumbricoides. This belief was based on therapeutic evidence and on stool examinations before and after treatment. Dr. França explains the mechanism of origin of urticaria-like disturbances thus: histamine by its action on skin capillaries induces a local congestion which increases parietal permeability, allowing an exudation of plasma. Giant urticaria occurs when the increased impermeability of the walls is sufficient to cause voluminous exudation, and when this increase occurs in such lean subcutaneous tissue as the eyelids and the ear, a pressure on the inner structure of the skin results. If attention is paid only to histamine liberation, one cannot be sure whether the skin disturbance is allergic or toxic, because the histaminic phenomenon is present in both cases. To make the distinction between these two types of disturbances more difficult, people with both disturbances benefit from antihistaminic therapy. There is apparently no relationship between the type and intensity of the disturbance on the one hand and the nature of the parasite and intensity of infestation on the other. When the stool examination of a patient with cutaneous manifestations is positive, one can suspect but not affirm that such a disturbance is a reaction to the parasitism. Final proof depends on cure of the skin condition by eliminating the parasites.

FRANCE

Poliomyelitis.—At a meeting of the Medical Academy of Paris in June, Professor Lepine reported that because the antibodies produced in the body by means of the poliomyelitis vaccine develop slowly, the injections should be spaced out. The best results appear from six weeks to two months after the third injection; 74% of vaccinated persons develop immunity; 10% show antibodies against poliomyelitis without vaccination. Natural immunity increases with age. Of the three types of virus, type 1 is the most dangerous. It causes the large epidemics, and is responsible for the most severe cases; 90% of the cases in France are caused by this type. The morbidity rate for this disease in France in the critical ages is 27.3 per 100,000 inhabitants. The geographic distribution is irregular. Mountainous regions and thinly populated areas are less severely hit than overpopulated areas. Children should be vaccinated at an early age because the incidence of poliomyelitis has doubled in France in the last 15 years.

A New Anticonvulsant.—After investigations which showed that in vitamin B_1 the thiazole grouping was capable of preventing ill-effects provoked by its pyramidic group, a general anticonvulsant action was attached to the thiazole fraction. This property is augmented by esterizing the secondary alcohol function of the molecule and stabilizing the product with ethanedisulfonic acid. This product, Hemineurine, was tested in therapeutic trials, by P. Royer (*Rev. méd. Nancy* 83:367, 1958). The principal indication for Hemineurine by mouth is represented on the one hand by all the state of manic excitement and anxiety and on the other hand by insomnia, but Hemineurine is most effective when given intravenously. In patients with delirium tremens the results were striking. One or two perfusions of 100 cc. were generally sufficient to bring about disappearance of oneirism in the course of therapeutic sleep, the diminution of tremor, and a return of the temperature to normal. Similarly, alcoholic drunkenness responds to this product in even the smallest doses. Epilepsy also constitutes an excellent indication for Hemineurine.

Sodium Liothyronine.—In a series of more than 100 patients, Linquette and co-workers (*Lille méd.* 3:243, 1958) found that the indications for therapy with sodium liothyronine and the results obtained with it were not perceptibly different from those of organotherapy and thyroxin. Generally, the results of treatment appeared much more quickly than with thyroxin, but for all that the benefit was not always apparent. Although sodium liothyronine has not caused any revolution in thyroid hormone therapy, it places at the physician's disposal a new, active drug with a flexible dosage.

SWITZERLAND

Galactosemia.—At the symposium on carbohydrate metabolism in Basel in June, Holzel of Manchester stated that the fact that the uridyltransferase is lacking and the galactose metabolism is disturbed in patients with galactosemia does not explain the varying severity of the clinical manifestations of this disease. Efforts have been made to explain this by saying that the uridyltransferase was only partially lacking, or that there are other metabolic pathways for galactose. To this can be added the functional maturity of organic systems that are usually directly or indirectly injured by the accumulation of the metabolite which is the phosphoric-l-glactose ester. The speaker cited the case of a child who, after a transient improvement, died of hepatic insufficiency as a consequence of total obstruction of the ductus choledochus by a bilirubin calculus.

Electroencephalographic studies in six children with galactosemia, as well as in their healthy sibs, produced normal tracings except in one boy who was not treated during the first 3½ years of his life. This patient had relatively frequent paroxysms that were indicated sometimes by focal phase inversions in the temporoparietal regions. The electroencephalographic tracings suggested multiple cortical epileptogenic foci. Regular observations of the mental development of these children showed that their IQ ranged from 85 to 100. The untreated 10-year-old-boy had an IQ of 60. Two of the children had seborrheic dermatitis, severe in one and subclinical in the other. One of the patients showed that in this disease all the tissues are involved. In addition to a mild form of this disease he also had hypothyroidism manifested only when he drank milk. At such times he had to be given thyroid extract. As long as a child with galactosemia is still growing, it is essential for him to follow a diet without galactose.

Hypoglycemia Precipitated by Amino Acids.—At the same meeting Payne and Woolf of London stated that in an earlier study the occurrence of hypoglycemia precipitated by the ingestion of proteins in young children was described. The authors studied the effects of a test dose of casein on the blood sugar. The result was an immediate fall in the blood sugar level. Further study of this phenomenon revealed that this fall was associated with an increase in the blood level of amino acids. Another protein, gelatin, was then used because its composition is notably different from that of casein. The ingestion of gelatin induced only a minimal fall in blood sugar levels but an increase in the amino-acid blood levels, similar to that seen after the administration of casein. The next studies were directed toward determining whether the induction of hypoglycemia was due to one or another amino acid contained in the proteins. Gelatin, by comparison with casein, contains practically no tyrosine, so this amino acid was tried, but no hypoglycemia occurred. Then leucine was tried, because casein contains 10% of leucine, whereas gelatin contains only 3.5%. The dose administered was equivalent to the quantity of leucine contained in the dose of casein given in the first trials. The fall in blood sugar was the same as that induced by casein.

Tests were then made to determine whether leucine itself or one of its metabolites had this hyperglycemia-inducing effect. The first product of degradation of leucine is a ketonic acid, which is not easily procured. The next product, on the other hand, isovaleric acid, is easily found. Consequently it was tested and it proved to be just as active as leucine. As for the final degradation products of leucine, they are now being synthesized because they are not available commercially. Attempts have been made to find out how leucine acts by studying, before and after the administration of this amino acid, on the one hand, the insulin-like properties of the blood, and, on the other hand, the difference between arterial and venous glycemias. For technical reasons, the results were not as convincing as the speakers might have wished. After the administration of leucine, the insulin activity of the serum was increased, as well as the arteriovenous gradient, which suggests that leucine increases the insulin activity in the serum. This may be due either to stimulation of insulin production or to inactivation of the insulin inhibitor contained in the serum.

Mechanism of Action of Glucagon.—At the same meeting E. Rossi and co-workers of Bern stated that they made a glucagon loading test using the intravenous route on 22 normal children ranging in age from 4 months to 13 years. The dose was 0.7 cc. per square meter of body surface (1cc.=1 mg.). After 10 minutes an increase in blood sugar values could already be seen; after 20 minutes the average increase in blood sugar was 52 mg. per 100 ml. above its initial value; after 30 minutes it was 59 mg. per 100 ml.; after 60 min. it was 28 mg. per 100 ml; and the glycemic curve generally returned to its initial level between the 60th and the 90th minutes. Pyruvic acid in the blood did not produce significant variations. The serum phosphate level declined sharply after 30 minutes. This test served as a subsitute for the epinephrine loading test, the results of which were not sufficiently exact because of the tachycardia, hypertension, and excitement induced by epinephrine which, moreover, was not satisfactorily absorbed because it was given subcutaneously.

In a second study an attempt was made to show how glucagon acts on the peripheral utilization of glucose. Blood was taken every 10 minutes for one hour from the cubital vein and also before and after venepuncture from the capillaries at the tip of the finger (capillary glycemia is comparable to arterial glycemia). Thus, it was possible to calculate the difference between arterial and venous glycemia. The peripheral utilization of glucose was better after glucagon and glucose, and especially after glucagon, glucose, and insulin than after glucose alone. These results confirmed the hypothesis that a synergy exists between glucose and insulin in the peripheral circulation.

Problems of Glucagon.—At the same meeting P. P. Foa and co-workers of Italy reported that glucagon is believed by some to be the hormone produced by the alpha cells of the pancreas and emitted in response to hypoglycemia, which it counteracts by producing hepatic glycogenolysis. This hormone would, then, be an integral part in blood sugar regulation and would have an action opposed to that of insulin. Others think that, on the contrary, glucagon puts glucose at the disposal of the tissues and thus has an effect synergistic with that of insulin. Glucagon is a polypeptide with a minimum molecular weight of 3,485. It contains 29 amino acids disposed in such a way as to exclude the possibility of its being an insulin product. The intensity and duration of its action are measured in animals rendered diabetic by alloxan, hypophysectomized, and adrenalectomized. Methods which have greater sensitivity are those using as an index the glycogenolysis or the reactivation of phosphorylase in liver sections or in homogenates.

It is almost certain that the alpha cells secrete glucagon, because it can be extracted from parts of the pancreas which contain alpha cells but not from the uncinatus process which does not contain alpha cells. Severe anoxia produces hyperglycemia and degranulation of the alpha cells in fish. Insulin treatment produces an increase in the glucagon content of the pancreas and the appearance of a hyperglycemia-producing and glycogenolytic factor in the blood of the pancreaticoduodenal vein. It seems that the hormone of the anterior hypophysis stimulates the secretion of glucagon by the pancreas. Administration of the growth hormone intravenously produces an immediate hyperglycemia in the normal or diabetic dog and in man. At the same time the speakers could stimulate in the blood of the pancreaticoduodenal vein the production of a hyperglycemia-producing and glycogenolytic factor; which, however, could not be identified as glucagon. It may be that it is a sympathicomomimetic substance, produced by the argentophil cells of the gastrointestinal mucosa, such as 5-hydroxytryptamine.

After the intravenous administration of tagged glucagon, the speakers followed its distribution in various organs and concluded that the liver and the kidneys were important organs in its degredation. In the plasma of the hepatic cells they found a ferment which inactivated glucagon, but this enzyme had only a limited specificity. It seems that glucagon is rapidly broken down, which renders it improbable that certain hyperglycemia-inducing and glycogenolytic substances found in the urine are derived from it.

The intensity and duration of the hyperglycemia due to glucagon varied with the experimental conditions. Simultaneously with this hyperglycemia, the glycogen content of the liver diminished greatly. After 24 hours the reconstitution of the glycogen content of the liver had taken place. This was attributed to the insulin reaction which was precipitated. This glycogenolytic action was associated with the formation of a ribonucleotide, which in the presence of adenosine triphosphate and of magnesium stimulates the production of phosphorylase beginning with dephosphophosphorylase. Because this effect is demonstrable not only in the sections but also in liver homogenates, it does not seem that the action of the hormone depends on an intact cell. The effect of the hormone on muscular glycogen is less certain. It seems that glucagon exerts only a moderate influence, if any, on the extrahepatic utilization of glucose. The continuous administration of glucagon produced hyperglycemia and glycosuria in dogs and in rats which lasted as long as the glucagon was being given. This diabetogenic action was reinforced by cortisone.

The fact that patients with diabetes have more alpha cells than have healthy subjects suggests the possibility that glucagon plays an etiological part in the pathogenesis of diabetes. Because of its capacity for producing temporary diabetes in animals and its influence on the nitrogen balance and on the metabolism of ketone bodies, the hypothesis that it has an etiological role in diabetes has been strengthened. Glucagon has been used to combat shock due to exogenous insulin, but it is not effective in hypoglycemia due to hyperinsulinism. Under given circumstances, it may be used as a liver-function test. The speakers believed glucagon to be an effective and quick-acting hormone which stimulates glycogenolysis according to the state of the available reserves of glycogen and which thus increases the blood sugar level. It is secreted as a response to hypoglycemia by the alpha cells of the islands of Langerhans, and in turn stimulates insulin production by the hyperglycemia which it provokes. The somatotrophic hormone may stimulate glucagon production, but this is not likely. Glucagon is secreted in the portal system and reaches the liver directly, which is not the case with epinephrine. Thus, glucagon is by its mode of action, by the site of its production, and by the complete absence of secondary effects absolutely designated to correct fluctuations in blood sugar, and it should be considered as forming an integral part of the mechanism of blood sugar regulation.

Acetonemia in Children.—At the same meeting H. G. Krainick of Freiburg-im-Breisgau, Germany, stated that early childhood is characterized by a marked predisposition to ketosis, which is manifested clinically by vomiting. One may determine which age group is predisposed to ketosis by subjecting children of different age groups to a fast of short duration and by observing the urinary elimination of ketone bodies. There is even in the nursling a certain predisposition to ketosis, but it cannot manifest itself by a severe ketonuria because of a greatly reduced renal clearance for ketone bodies. One may also demonstrate the predisposition of young children to ketosis by giving them epinephrine, which regularly produces an increase in ketone bodies in the blood. The hyperacetonemia due to epinephrine is particularly marked in patients with latent ketosis, which may be brought to light in this way. The speaker concluded that ketosis precipitated by epinephrine is due partly, if not completely, to a diminution of ketone body utilization in the peripheral tissues, which is caused by the epinephrine. In a series of children with typical acetonemic vomiting (which it would be more appropriate to designate as ketonemic crises), he studied the level of the ketone bodies and of the sugar in the blood during treatment. He observed a tendency of ketosis to contiue for a long time (in some cases up to five days) after cessation of vomiting, in spite of a continuous supply of glucose, liquids, and electrolytes—a finding contrary to that observed in other conditions of hyperketonemia. Hypoglycemia was not pronounced, the average blood sugar level being 67 mg. per 100 ml. In comparison with the ketonemic crises, ketosis which is associated with hypoglycemia, properly speaking, never reaches a high degree.

Hypoglycemia does not appear to play a causal role in the pathogenesis of ketonemic crises. The chief cause really resides in an overproduction of ketone bodies (hyperketogenesis). This in turn would be primarily the result of an over-rapid mobilization of fat. Vomiting and hyperketonemia in the course of the ketonemic crises do not depend on one another but must be considered as parallel manifestations of the same irritation of the central nervous system. The possibility that hyperketonemia may be of central origin is suggested by the fact that different hormones of the anterior lobe of the hypophysis have a ketogenic activity. It was possible to demonstrate in 26 healthy children the ketonemic-inducing effect of ACTH. The principle that mobilizes fats and favors ketosis resides in the anterior hypophysis. The frequent modifications of the electroencephalogram encountered in such children also speak in favor of the central origin of the ketonemic crises.

Civil Defense.—The International Organization for Civil Defense met in May in Geneva. This nongovernmental organization is composed of the various national civil defense associations. The conference brought together the delegates of 27 countries, including the United States and Russia. The risk that our civilization would run while attempting to defend its existence with atomic weapons constituted the essential preoccupation of the meeting. The main subjects for discussion were the protection of the population in the course of an atomic bombardment and the establishment of an international center for registration and warning against radioactivity. The protection of civil defense personnel in time of war and a project for the establishment of insurance against the damage that might be caused in time of war to historical and cultural monuments were also considered. The United Arab Republic's delegate ventured to state that discussion of protecting cultural possessions is useless if one does not at the same time outlaw atomic warfare. The role of the International Organization of Civil Defense is not that of a judge but that of an informant. A conference like this can only point out dangers and indicate the possible means of protection.

Prof. Jentzer of Geneva speaking of warning against radioactivity stated that not only atomic bombs but also atomic industrial wastes cause a dispersion of radioactive debris. These products contaminate air, earth, and water and thus the plants and the animals that serve as food to man. Certain countries are already regularly measuring the amount of radioactivity in the air, water, and soil. A central information agency is needed which, on the basis of data collected in different countries, would be able to give timely warning to the civil defense services of threatened or contaminated regions. These services could, in turn take appropriate measures to protect the population by directing evacuation and prohibiting consumption of contaminated food. Such a center should be established by an international agreement between the governments of as many countries as possible. It should not be limited to one bloc, because only by the world-wide extension of this agency could it be truly effective and able to protect multitudes of human lives from destruction by radiation. The basis for the activity of the center would be the setting up of a world map of radioactivity. Thanks to a network established between the national registration centers, a network similar to that of the meteorological stations, the center would receive information on the procedures put into effect in various countries. This proposal met with unanimous approval by the delegates, and a recommendation was sent to the World Health Organization asking their collaboration in establishment of such a center.

General Dr. Sillevaerts, president of the Belgian Superior Council of Civil Defense, said that in all atomic explosions the effects of blast, heat, and radiation must be considered. The only means of protection against bombardment of any kind are distance and shelter. Ordinary cellars, or even a deep narrow dry ditch, may give complete protection from the blast and the heat of an explosion and relative protection from its initial radiation. In fact these simple devices are sufficient at distances of a few hundred yards from ground center, for a bomb of the type exploded at Hiroshima, and about 1.4 miles for a hydrogen bomb. Earth and concrete give excellent protection, but the maximum total dose of whole body radiation which it is now believed that a person can endure without somatic damage does not exceed 25 r, and this figure is largely exceeded in shelters near the point of impact. The organization of civil defense in a threatened population agglomeration should include not only the installation of shelters in premises but also plans for evaluation and dispersion of the population. Evacuation means the transportation of mothers, young children, and old people (about 30% of the population) to distant rural areas. Dispersion means the grouping of indispensable personnel, of either the sanitary or civil defense organizations, and of employees of vital services and factory workers occupied in producing war material (about 20% of the population) in the peripheral areas of the agglomeration, which are less exposed to the dangers of bombardment.

Shelter, evacuation, and dispersion bring up the problem of warning. The period between the giving of the alarm and the explosion of the bomb is becoming shorter and shorter as techniques of offense advance. Experts agree that rockets and guided missiles have shortened this period to about one minute. It would be scarcely possible, in case of an atomic alarm, to reach a shelter on one's own premises, and every passer-by surprised in the street by the siren would be practically condemned. Moreover, a formal declaration of war is a thing of the past. Evacuation and dispersion require several days, and they should therefore be carried out during the period of tension preceding the onset of hostilities. In the present state of chronic tension, what government would be able to recognize the seriousness of a recrudescence and take the responsibility for such draconian measures?

On the other hand, the radioactive fallout following explosion constitutes a serious menace. This fallout consists of extremely minute particles projected into the stratosphere which may not settle to earth for years after the detonation of the bomb and coarser particles which settle within a few days after the explosion and possess great radioactive intensity. Geographically, this cloud assumes the form of a cigar pointing in the direction of the prevailing wind and may extend for several hundred miles. A system for registration and coordination of information should therefore be established to make it possible to advise the population in regard to the precautions to be taken. In densely populated, threatened areas, disaster-relief and fire extinguishing services should be installed around the critical target areas, that is, in the zones of moderate and slight devastation 1.5 to 2 miles from the point of maximum impact for the classic atomic bombs and from 9 to 12 miles for hydrogen bombs. This simple statement of the distances that must be traversed by the relief services gives an idea of the effectiveness that can be expected from them insofar as radioactivity permits access into the disaster areas. In practice only the slightly wounded who were themselves able to go to the posts of the relief services could benefit by any aid other than the mutual help given by one wounded person to another.

The conference recommended to the various governments the initiation of a vast civil defense program which would be effective in case of atomic warfare. In addition, the conference created a committee of investigation, the main purpose of which is to redefine on the basis of present data the exact mission of civil defense in the face of the new risks presented by radioactivity in times of war, principally as regards the genetic hazards.

UNITED KINGDOM

Childhood Malignancies.—Alice Stewart and coworkers (*Brit. M. J.* 1:1496, 1958) conducted a survey of malignancy in childhood. An attempt was made to trace 1,694 children who died of leukemia or cancer before their 10th birthday. The parents and doctors of 83.6% of these were traced and data obtained on the prenatal and postnatal experiences of the children, which were compared point by point with the experiences of a similar group of live children that served as a control. The same physician treated the child with leukemia or cancer and the one who served as a control. The frequency of direct fetal irradiation, virus infections, and threatened abortion was significantly higher in the children who died from malignancy than in the live control children. Excessive maternal age appeared to increase the risk of leukemia in childhood, and this disease and mongolism tended to occur together. The frequency of roentgen irradiation in infancy, acute pulmonary infections, and severe injuries was significantly higher in the case of children who subsequently died of leukemia than in other children. The health of the mothers and the home background of the children were not significantly different in the two groups. The authors concluded that fetal irradiation does not account for the recent increase in childhood malignancies, but they believed that x-ray examinations and treatments should be reduced to the absolute minimum in pregnancy and childhood.

Diet and Arterial Disease.—Attention has been focused more on an excess of fat in the diet than on an excess of food as a factor in the cause of atheromatous arterial disease. Keen and Rose (*Brit. M. J.* 1:1508, 1958) examined the diets of 10 men and 14 women with atheromatous disease, including angina pectoris, cardiac infarction, and intermittent claudication, and compared them with those of randomly selected control subjects, matched for age, sex, and race. An analysis was made of the food eaten by all subjects. Body measurements showed the atheromatous subjects to be a little shorter and heavier than the controls, and there was a slight tendency for caloric intake to increase with body weight. It was found that the atheromatous men were bigger "all-round" eaters than the male controls, whereas the athermatous women were bigger eaters of fat only. The atheromatous patients of both sexes showed a higher intake of each of the main foodstuffs. The atheromatous men's caloric intake was 24% higher than that of the male controls. Their mean consumption of carbohydrate was 20%, of protein 26%, and of fat 28% greater. In the case of the women the atheromatous subjects also showed a higher caloric intake, but the excess (9%) was smaller than that of the men, and this was derived almost entirely from fat, the consumption of which was 24% above that of the female controls. The carbohydrate and protein intake of the atheromatous women was practically the same as that of the female controls. The intake of fat of the atheromatous group as a whole was 28% greater than that of the normal group. When the figures for total fat intake were broken down in the proportion of their constituent saturated and unsaturated fatty acids, the atheromatous men ate an absolute excess of all fractions, as compared with the male controls, but they consumed a rather higher proportion of their fat in a saturated form and a lower proportion as polyunsaturated fatty acids. There was no evidence that a deficiency of unsaturated or long-chain fatty acids was an important etiological factor, as has been suggested.

Reduction of Benzpyrene in Tobacco Smoke.—The annual report of the Tobacco Manufacturers' Standing Committee of Britain described the work carried out in the industry's laboratories to discover substances to reduce the amount of benzpyrene in tobacco smoke. The claim that the impregnation of cigarette paper with 4% ammonium sulfamate is effective for this purpose was not substantiated, although this compound was effective when added in large quantities to the tobacco itself. Two other substances were discovered, copper nitrate and platinum diaminonitrite, that reduced the benzpyrene in tobacco smoke. The latter, unless effective in infinitesimal amounts, is likely to prove too expensive a remedy. Besides benzpyrene a number of other polycyclic hydrocarbons have been found in tobacco smoke, and they are being investigated. Now that arsenical insecticides are no longer used to spray tobacco crops, traces of arsenic, which might be carcinogenic, have almost disappeared from cigarettes made in Britain. A new research project, the examination of smoldering combustion, particularly in relation to forced air supply in such products as tobacco, is under way.

Electrocardiogram.—Davies (*Brit. Heart J.* 20:153, 1958) questioned the reliability of the electrocardiogram in the diagnosis of cardiac conditions. He submitted 100 electrocardiograms to 10 observers, 9 of them cardiologists and one a general practitioner, for their opinion. They were asked to report whether they were normal, abnormal, or showed evidence of infarction, but they were given no clinical details of the patients. Each observer was given the same tracings to examine twice, with an interval of a fortnight in between. Not only was there a wide divergence of diagnostic opinion between the different observers but also there was a great variation between the first and second reports of individual observers reading the same electrocardiograms. The general practitioner showed the greatest inconsistency in his first and second reports and the greatest disagreement with the reports of others. Of 100 tracings a unanimous report was given on only 29; 67% of the reports agreed on 49 tracings; and less than 67% agreed on the remaining 22. The disagreements on the first and second reports of the same observer varied in the case of between 7 and 33 of the 100 electrocardiograms submitted. This study shows the diagnostic limitations of the ECG, particularly when a single tracing is seen and interpreted without the history, age, sex, and background of the patient. It also emphasizes the need for special training in cardiology for the interpretation of electrocardiograms.

Absence of Parents During Childhood.—Possible long-term effects of separation of the child from its parents are reported by Oswald (*Brit. M. J.* 1:1515, 1958), who collected statistics from Royal Air Force personnel aged 18 to 29. In many cases the separation occurred during the war years, when as children they were evacuated from the towns because of air raids or separated from the father who did war service. Significantly more of those with psychiatric diseases had a history of separation from their parents when young than did other medical patients, such as those with epilepsy, head injury, or some neurological condition. There was no significant difference between a group responsible for accidents who gave a history of separation from parents and a control accident group with no such history.

Diets in Pregnancy.—Miss Helen Simpson, the dietitian to the Simpson Memorial Maternity Pavilion of the Edinburgh Royal Infirmary, stated in her annual report that there has been a noticeable deterioration in the diets of many women, particularly in pregnancy. The deterioration is attributed chiefly to the increased cost of living and to a rise in unemployment. In some families, although the income would appear adequate, credit commitments resulted in less being spent on food. The consumption of the most expensive foods, namely those rich in protein, was reduced in favor of the cheaper carbohydrate foods, with which appetite was satisfied. One result of a lowered intake of meat and protein foods was an increase in the incidence of anemia in women. The pint of milk provided at half price to the pregnant woman tended to be shared with the family. Less fruit and vegetables were eaten by those in the lower income group. A woman might start her pregnancy in good health, but her condition often deteriorated toward the end of it, as she often became anemic on an inadequate diet. It was necessary to give iron to a number of the women to correct anemia.

Health Service Criticized.—The National Health Service was criticized in a recent debate in the House of Lords. Lord Moran, formerly President of the Royal College of Physicians, said that there is great discontent among general practitioners with the health service. This is partly financial, as the doctor can only increase his income by taking on a bigger panel of patients than he can properly care for, but the chief cause is to be found in the decline in the status of the general practitioner, which began when people generally felt that when they were seriously ill they were well advised to go to hospital. It was mortifying to the physician to find that the patient no longer put his trust in him and preferred to be treated at the hospital by a stranger. The health service exaggerates this because there are now specialists in every field of medicine and surgery, and the general practitioner no longer has access to hospital beds as he used to. The good general practitioner often had semispecialist experience and previously had a hospital appointment. This made his work more interesting. The remedy would be to give hospital appointments to the best general practitioners so that they could treat at least some of their patients in hospital. If this is not done, the profession will continue to be discontented and efficiency will diminish, whatever the remuneration. Lord Moran was not happy about the quality of the students admitted to medical schools today. Formerly they came from the middle class and their expenses were paid for by their parents. Today the state pays most of their expenses, and they are selected by examination without any test of, or regard to, character.

The inadequate provision for the teaching hospitals was criticized by Lord Evans, the Queen's physician, who said that they are mostly outmoded, with inadequate accommodation for patients, teaching, and research. Of 12 teaching hospitals in London, only 2 have been rebuilt in the last 25 years, although many were badly bombed during the war. In the past, much of the success of the hospitals was due to their complete freedom. This freedom is curtailed today in many ways. For example even to employ an extra kitchen-maid requires permission from the Ministry of Health. The so-called merit or distinction awards given to some specialists were strongly criticized by Lord Uvedale, a Socialist peer and a physician. They cost the state $5,600,000 a year, and their secret award is contrary to public policy. Nobody except the Ministry and the recipients know who gets these awards. When public money is spent the public should know how and why. Lord Pakenham called attention to the 10,000 old people occupying beds in mental hospitals because there is nowhere else for them to go. This is a waste of valuable bed space. They do not need skilled mental treatment, but they need additional residential accommodation. The Royal Commission on Mental Laws had recommended that local authorities should make provision for the elderly infirm who did not need hospital treatment.

Prednisone and Cancer of the Breast.—The effects of prednisone in a group of 29 patients with advanced cancer of the breast were studied at the Westminster Hospital, and the results were summarized in the annual report of the British Empire Cancer Campaign for 1957. The patients had all received treatment according to the stage of the disease on presentation (radical surgery, irradiation, or both). They had been followed up and given further irradiation, androgens, or estrogens, as the disease progressed. Finally, when their condition was no longer controlled, they were given a trial of therapy with prednisone at a dosage of 20 mg. daily. The ages of the patients ranged from 37 to 81, and the duration of treatment varied from one week to seven months. Twelve patients were still alive and on treatment when last seen; 18 showed definite relief from pain due to skeletal deposits, improvement in cough and dyspnea associated with pulmonary deposits, and improvement in general well-being; 9 showed definite improvement in the radiologic appearance of skeletal and pulmonary metastases and regression in the local breast condition or in skin deposits; and 12 of the 18 patients who showed a good subjective response had previously shown sensitivity to estrogens or androgens. Three patients had shown no sensitivity to estrogens or androgens. There were few side-effects.

Epidemiology of Cancer.—An exhaustive statistical survey of cancer in North Wales (largely rural) and in the Liverpool region (largely urban), carried out in the five years 1952 to 1956 by Dr. Percy Stocks, was published as a supplement to the annual report of the British Empire Cancer Campaign. Standardized mortality in the period 1947 to 1954 from cancer of the stomach, taking the national figure as 100, exceeded 150 in 26 of the 54 communities of North Wales, ranging from 200 to 260 in 9 of these; but it exceeded 150 in only 2 of the 33 areas in Cheshire and Liverpool. The standardized death rate in the period 1952 to 1955 for cancer of the lung was two and one-fourth times as great in Liverpool as in North Wales. The incidence of gastric cancer, but not of intestinal cancer, was correlated with the reported frequency of having eaten fried foods during 20 years before the onset of the illness. Frequent beer drinking, reported as having been habitual during 20 years, was correlated with nongastric cancers, the correlation with lung cancer being strong among light smokers but absent among heavy cigarette smokers. Frequent milk drinking was correlated with an absence of lung cancer in the Liverpool region, no matter what the beer-drinking and smoking habits of a subject were. Frequent tea drinking by men was correlated with an absence of cancer among heavy beer drinkers and all grades of smokers in Liverpool, but no such association was found in Wales. Frequency of eating green vegetables was reported as peculiarly high in certain parts of North Wales and was there correlated with an absence of cancers except of the breast.

Female hospital patients with lung cancer in Liverpool showed a significant excess of smokers compared with controls, but those with gastric and mammary cancers in North Wales and Liverpool did not differ from the controls in respect to smoking history. Among 255 women who died of lung cancer, 108 had smoked, compared with 50 expected from women of the same ages who died in the same districts of gastric and mammary cancers. Among 576 male hospital patients with lung cancer the ratio of nonsmokers to the number expected from the noncancer controls was 1:7; for pipe smokers it was 1:2; for smokers of up to 50 cigarettes a week 1:1; and for heavy cigarette smokers 4:3. The rates of inception of lung cancer at ages 35 to 74, standardized by the national census population, were in pipe smokers 2 to 2.5 times, and in cigarette smokers 4 to 5 times, the rates among nonsmokers. The urban/rural ratio between the inception rates was about 2.5:1 for nonsmokers and light cigarette smokers, 3:1 for pipe smokers, and only slightly above unity for heavy cigarette smokers.

Among 2,101 men aged 35 to 74 who died of lung cancer, 40 had not smoked compared with an expected figure of 188 based on the 1,155 men of the same ages and living in the same districts who died of gastric cancer; 1,285 had smoked up to 150 cigarettes a week compared with 1,260 expected, and 593 had been heavier cigarette smokers compared with 325 expected. Nonsmokers, pipe smokers, and light cigarette smokers showed upward gradients of the standardized death rate in passing from the most rural to the most urban area, but heavy cigarette smokers did not. The urban/rural ratios were 2.3:1 for nonsmokers, 2.5:1 for smokers of up to 100 cigarettes a week, 1.8:1 for pipe smokers, 1.7:1 for medium cigarette smokers, and 1:1 for smokers of 200 or more cigarettes a week. The regression lines of mortality on maximum number of cigarettes ever smoked every week habitually ran parallel up to about 200 weekly for the different geographical areas, but the urban graph of Liverpool then ceased to rise further, suggesting that despite great exposure to irritant factors not all men were susceptible to lung cancer. Among nonsmokers living continually in rural surroundings the male and female death rates were about equal. Measurements of air pollution showed that the incidence of lung cancer in nonsmokers and light smokers corresponded in general with the pollution levels, but insufficient data were available to incriminate any particular substance. Pipe smoking, which increased the risk of lung cancer only slightly, was associated positively in the Liverpool region with the incidence of cancers of the larynx, esophagus, intestine, and rectum and in North Wales with cancers of the larynx, esophagus, and intestine except the rectum.

The mortality from gastric cancer in England and Wales was high where igneous rock was near the surface and low in chalk and limestone areas, and in the survey region the rates tended to be highest where strata of the Cambrian age outcropped. In certain areas garden soils where a person died from gastric cancer after 15 or more years' residence had higher median concentrations of zinc and chromium than garden soils in the same areas where a person died from a cause other than cancer or died of cancer after a residence of less than two years. No statistical relation with cancer was found for cobalt, titanium, vanadium, lead, or iron, but nickel was associated with an absence of cancer. In the Welsh districts with a high death rate from gastric cancer, but not elsewhere, the incidence of gastric cancer after 10 to 19 years of residence was excessive where the garden soil had a high content of organic carbon and was still more excessive after 20 or more years of residence where the soil had a medium organic carbon content. Similar relations appeared with the loss on ignition and with invertase activity of the dried soil. No such correlation was found between garden soils and cancer of other organs. Something in the soil yet to be identified appeared to be the main factor responsible for the peculiarly high incidence of gastric cancer in parts of North Wales. No positive associations were found between cancer incidence and the use of oil lamps for heating or lighting, the use of petrol lighters for smoking, or a past history of streptococcic infection or vaccination.

Gastrectomy and Loss of Weight.—Johnson and coworkers (*Lancet* 1:1242, 1958) studied a series of 209 patients who had undergone gastrectomy of various types. They found that, on the whole, those who had lost much weight before operation tended to regain it after, and those who had maintained their weight and the few who had gained weight up to the time of operation tended to lose it afterwards. Thus, of the 170 patients who underwent partial gastrectomy with a Polya-Finsterer anastomosis for peptic ulcer, 57% had remained within 15 lb. of their weight in health up to the time of operation. On the average they lost 3 lb. (1.3 kg.) before operation and another 4 to 6 lb. (1.8 to 2.7 kg.) afterwards. The 42% who lost 15 lb. (6.8 kg.) or more (average 35 lb., or 15.9 kg.) before operation gained an average of 20 lb. (9.1 kg.) after operation but remained a little lighter than those in the previous group. About 1% gained 15 lb. (6.8 kg.) or more (average gain 43 lb., or 19.5 kg.) but lost 20 lb. (9.1 kg.) after operation and remained well above their weight in health. An analysis of two groups of 15 patients, one with normal weight and one underweight, who had undergone subtotal gastrectomy for peptic ulcer at least a year previously showed that those with normal weight were getting an average of 102% of the calories which theoretically they needed and that those with low weight were eating only 76% of this amount. The severity of postcibal symptoms was much greater in those who were underweight.

A group of 40 patients who had lost 14 lb. (6.4 kg.) or more since partial gastrectomy for peptic ulcer at least two years previously were allocated at random to six groups for treatment: control; iron given intramuscularly; vitamin B_{12} given intramuscularly; dietary supervision; 25 mg. a day of methyltestosterone given sublingually; and 50 mg. of iproniazid daily by mouth. No significant change was observed in the control group or in the groups who received iron or vitamin B_{12} intramuscularly. Significant gains in weight were found in those who had dietary supervision, methyltestosterone, or iproniazid. Dietary supervision increased the weight in every case, but the results with methyltestosterone and iproniazid were less consistent. Of the seven patients (all men) who received methyltestosterone, two gained 8 lb. (3.6 kg.) in as many weeks, one gained nothing, and one lost a pound (0.5 kg.). No side-effects were observed. Of the seven patients who received iproniazid, all gained weight, one gaining 10 lb. (4.5 kg.). The mean gain in weight was 4.3 lb. (1.95 kg.) for patients given dietary supervision, 4.4 lb. (2.0 kg.) for those given iproniazid, and 3.7 lb. (1.65 kg.) for those given methyltestosterone. In an additional group of nine men treated with a combination of dietary supervision and methyltestosterone, the mean gain in weight at eight weeks was 6.2 lb. (2.8 kg.).

Phenylbutazone in Rheumatic Disease.—Phenylbutazone has now moved up to second place (after aspirin) on the list of possible drugs for routine use by outpatients with rheumatoid arthritis, according to Mason and Hayter (*Practitioner* 181:23, 1958). An analysis of the records of a sample of 335 patients with rheumatoid arthritis, representing all those with this disease seen in a three-month period, showed that 67.2% had at some time been given phenylbutazone. It is now being prescribed earlier in the course of the disease. Thus, in 1952 only 22% of those given the drug had a disease duration of less than three years, whereas in 1955 and 1957 70% and 68%, respectively, had such a history. Since 1954, only an occasional patient has had a dose larger than 400 mg. a day. Phenylbutazone should normally be given a trial before embarking on deep x-ray therapy in patients with ankylosing spondylitis. It is particularly useful for women of childbearing age. Smaller doses are more effective in this disease than in others, many patients being controlled with 200 or even 100 mg. a day. It is of especial value in osteoarthritis of the hip where, by permitting the proper use of the joint in allowing smoother walking, it may prevent the development of contracture and deformity. Nocturnal pain is also conveniently relieved owing to its prolonged action. Phenylbutazone may supersede colchicine in the treatment of acute gout. This is the only condition in which these authors use a dose in excess of 400 mg. a day, preferring 600 mg. a day until the acute attack is controlled, usually within two or three days, after which 400 mg. a day is sufficient until the attack has completely subsided.

Toxicity was never a serious problem. About 65% of the 225 patients with rheumatoid arthritis had only transient side-effects, if any. Those who tolerated the drug well showed a better symptomatic response than the rest. Thus, 87.8% of the nontoxic group claimed some symptomatic relief, compared with 60.3% of the toxic group, and 42.2% of the former and only 16.7% of the latter had excellent or good relief. About 67% of the toxic reactions were gastrointestinal; 25% developed a rash; and buccal ulcers and stomatitis were relatively uncommon. In general, toxic effects appeared early; 60% appeared in the first six weeks of administration. The onset of gastrointestinal reactions, however, was often delayed, and three patients developed peptic ulcers after two years' medication. Treatment with phenylbutazone should never be reinstituted in a patient who has once had a toxic reaction.

Streptomycin Dermatitis in Nurses.—Dr. Harold Wilson (*British Medical Journal,* June 14, 1958) cited a report from the Ministry of Health (1953) which stated that nurses have become sensitive to antibiotics in spite of strict adherence to careful technique and the wearing of gloves, gowns, and masks. During the period of observation, however, over 100,000 injections of streptomycin were given in two wards by nurses wearing gloves and masks without the occurrence of a single case of dermatitis. Where these precautions were not strictly observed the incidence was about one case per 4,000 injections. The author believes that streptomycin dermatitis in nurses could be reduced to a minimum either by their wearing gloves and masks before giving injections or by their avoiding direct contact with the drug through the use of cartridges as described by Howells in 1956. Most chest physicians adopt these precautions as a routine measure. In general wards, however, where streptomycin is used sporadically, the dangers of dermatitis are not fully appreciated and insufficient care is taken by those handling the drug. If possible the streptomycin-sensitive nurse should be given work where she will not come into contact with this drug. If this cannot be done desensitization should be considered. This is a tedious procedure and not without risk. It is definitely unsafe in inexperienced hands, as most persons develop a reaction at some stage in the course. Corticosteroid cover or the use of repeated minute doses in place of the conventional method may reduce these reactions but is not likely to eliminate them altogether.

Mass X-Ray Survey.—Practically 300,000 films were taken in the mass x-ray survey of Edinburgh. As a result, 216 patients were discovered who needed treatment in hospital, 126 of whom could be treated while at work. In addition, there were 810 who had no signs of active disease but will be kept under observation and 150 who were referred for investigation of other chest diseases. Half the new patients were young people, and most of the others were old men. Hundreds of beds had been prepared at the beginning of the survey to deal with new patients, but the number of patients with active tuberculosis appears to have been overestimated.

Cravings of Pregnancy.—A series of 991 pregnant women with food cravings and of 193 with food aversions was analyzed by Harries and Hughes (*Brit. M. J.* 2:39, 1958). Fruit was craved by 261 women. The commonest fruit craving was for apples (76 patients), and most of those with this craving wanted sour ones. The most interesting feature of the analysis was the list of cravings for substances other than food. This included coal (35), soap (17), disinfectant (15), toothpaste (14), tar (10), and cinders (4). The list of aversions included tea (78), smoking (24), coffee (22), and beer (4).

CORRESPONDENCE

DRUG REACTIONS

To the Editor:—In our recent article on the treatment of idiopathic thrombocytopenic purpura (ITP) with prednisone (*J. A. M. A.* 166:1805-1815 [April 12] 1958), we noted in an addendum that two additional patients with ITP treated with triamcinolone showed excellent hematologic responses. Further observations indicated that the latter product had hematological effects resembling closely those obtained with prednisone. Subsequent use of this product indicates that in the relatively high doses required in our patients, a rather high incidence of a variety of nonhematological reactions occurred. As a result, we are reappraising its usefulness when administered in the dosages required for the therapy of the various hematological disorders. Sixteen consecutive patients with hematological disease (ITP, autoimmune hemolytic anemia, and leukemia) were treated with triamcinolone in maximal dosages varying from 12 to 100 mg. daily. The latter dosage was used in only one patient (with severe autoimmune hemolytic anemia); in six others, the maximal dosage was either 64 or 72 mg. daily. In the rest it was 40 mg. or less daily. Of the 16 patients treated, untoward reactions occurred in eight and minor reactions in four. In four, no deleterious effects were observed; in these, the maximal dosage used varied between 12 and 40 mg. daily. The following reactions were observed.

Muscle Weakness.—Muscle weakness occurred in three women and one man, all of whom had autoimmune hemolytic disease. No indications of systemic lupus erythematosus were present. The weakness involved particularly the quadriceps muscles bilaterally and resulted in difficulty in walking, particularly up and down stairs. It appeared in two to four weeks after treatment with the drug was started and was unassociated with reflex disturbances. Slight atrophy of the quadriceps group was observed in two of these patients. Hypopotassemia was not observed but was present in another patient reported on below. The maximal daily dosage of triamcinolone used in these patients was 64, 32, 72, and 72 mg. respectively. When potassium was given and prednisone substituted for the triamcinolone in somewhat smaller dosages (40, 30, 50, and 50 mg., respectively), the muscular weakness subsided gradually in a period of two to eight weeks, with continued hematological improvement.

Hypopotassemia.—Hypopotassemia occurred in one patient with autoimmune hemolytic anemia and a previously mild diabetes mellitus not requiring insulin. This patient was given 64 mg. of the drug daily for 10 days, then 32 mg. daily for two weeks, then 24 mg. daily. She was admitted to her local hospital in a semicomatose state, with marked flushing of the skin, swelling of the face, and inability to walk because of quadriceps muscle weakness. The hemoglobin level was 14 Gm. per 100 ml., blood sugar level 280 mg. per 100 ml., and serum carbon dioxide content 20 mEq. per liter. The serum potassium level was 2.6 mEq. per liter. Parenteral fluids, including potassium given orally and intravenously, insulin, and supportive measures were given. Triamcinolone therapy was discontinued. There was rapid improvement. One week later the patient's condition was greatly improved, and the serum potassium level was 3.6 mEq. per liter. The autoimmune hemolytic anemia was kept under control with maintenance doses of prednisone.

Bleeding Peptic Ulcer.—Bleeding peptic ulcer occurred in one patient, aged 65, with chronic lymphocytic leukemia and severe autoimmune hemolytic anemia, who was treated with triamcinolone in doses up to 100 mg. daily. Prophylactic management for peptic ulcer was carried out, although there was no history of ulcer. The hemolytic anemia was improving consistently, but the patient suddenly developed an almost exsanguinating gastrointestinal hemorrhage three weeks after triamcinolone therapy was started. An emergency gastrectomy after several transfusions was followed by death. A bleeding ulcer of the duodenum was found.

Severe Staphylococcic Infection.—One patient with myelofibrosis and myeloid metaplasia, severe anemia and thrombocytopenia, and a peculiar hemorrhagic disorder was treated with 72 mg. of triamcinolone daily. After one week of therapy, he developed a severe staphylococcic infection beginning on the lower lip, which soon involved the entire mouth. The drug therapy was discontinued, various antibiotics were given, and the patient eventually recovered from the infection. The incidence of drug-resistant staphylococcic infections in our area was high during this period.

Cardiac Failure.—A woman aged 48, with aplastic anemia of 10 years duration, was given 20 mg. of triamcinolone daily for about eight weeks. She had had no history or objective findings of cardiac or renal disturbance. In the ninth week of therapy she developed severe dyspnea, increasing edema, at first of the face but later involving the entire body, and all the indications of heart failure. The serum potassium level was normal. The drug therapy was discontinued, treatment for the heart failure was instituted, and the patient was relieved.

Minor reactions.—A lobster-red flush of the trunk occurred in two patients, and marked facial rounding without other symptoms occurred in two others. Most of the patients complained of some loss in weight, but in two there was a moderate increase in weight.

The large number of reactions occurring in this small series of patients may have been purely fortuitous, and in a second series perhaps relatively few reactions would take place. Similar reactions with other corticosteroids are, however, common. We have been impressed by the unusual frequency of the reactions and with the common occurrence of quadriceps muscle weakness. Since severe hypopotassemia was present in one patient and since no neurologic deficit was ascertained in any of them, it is theoretically possible that a tissue metabolic defect involving certain muscle groups occurred. This should be studied further.

The use of prednisone was followed by improvement of the muscular weakness, which might indicate a specific effect of triamcinolone in inducing this disturbance. Another even more specific effect of the drug was the development of marked erythema of the trunk, not seen previously with any of the other corticosteroids. The most severe reactions occurred when doses of 64 to 100 mg. daily of triamcinolone were given. In four patients in whom smaller doses of the drug (12 to 40 mg. daily) were used, reactions did not occur. This suggests that the drug should be studied further before it is used routinely in conditions requiring relatively large doses, in autoimmune hemolytic anemia, ITP, and other hematological disorders.

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SPACE MEDICINE

To the Editor:—In his stimulating and challenging president's address, "Physicians to the World," Dr. Gundersen (*J. A. M. A.* 167:1059-1076 [June 28] 1958) may have inadvertently given an erroneous impression when he said "with man probing into outer space, it appears that our scientific future will be further complicated by the development of still another specialty—space medicine."

Space medicine is not another, or new, specialty but a natural progression of aviation medicine. On Nov. 10, 1948, a symposium on "Aero Medical Problems of Space Travel" was held at the United States Air Force School of Aviation Medicine where, shortly thereafter, a department of space medicine was established. A second such symposium was held in Chicago on March 3, 1950, under the sponsorship of the University of Illinois, and on May 31 of the same year the Space Medicine Branch of the Aero Medical Association was founded. In the definition of aviation medicine, the United States Air Force Dictionary states: "'Aviation medicine' is used as an inclusive term, embracing both aeromedicine (in its restricted sense) and space medicine." Recently, in the June, 1958, issue of *Aeronautical Engineering Review*, Dr. Hubertus Strughold, who has been called "the father of space medicine," spoke of "space medicine—a branch or extension of aviation medicine."

In 1953 aviation medicine was officially recognized as a specialty, and certification by the American Board of Preventive Medicine was authorized. New aeromedical problems have arisen continuously since man achieved the power of flight, and it is not unreasonable to assume that future candidates for certification in aviation medicine will be expected to know of the solutions to some of these problems as they relate to space travel.

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ALIENS AND TUBERCULOSIS

To the Editor:—An editorial on aliens and tuberculosis appeared on page 1505 of the July 19, 1958, issue of The Journal. After having had a small amount of experience with the results of the relaxation of immigration laws I am of the opinion they pose a potential, if not an actual, public health threat to the United States. While great strides are being made in the eradication of tuberculosis, we can say that the battle is far from being won.

In the above-cited article is mentioned one phase of the immigration law (P. L. 85-316) that allows the admission of tuberculous aliens. Another phase is that this law does not prohibit the immigration of a child adopted in a foreign court by a family residing in the United States represented there by proxy. In effect, this means that a child so adopted can enter the United States as a citizen on a nonquota basis regardless of its physical condition. It has been reported that an individual living in Oregon has brought several hundred Korean-Caucasian children into the United States. Not only does this pose sociological and legal problems, but some of these children were admitted with tuberculosis. Those in my health jurisdiction will be kept under surveillance.

I have no way of knowing how many tuberculous aliens are entering the United States. However, serious consideration should be given as to how they will affect our tuberculosis picture.

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LAW DEPARTMENT

MEDICOLEGAL ABSTRACTS

Revocation of License for Offense Involving Turpitude.—This was an action to review the revocation of a physician's license following his commission of a crime involving moral turpitude. From an action in the superior court affirming the action of the medical disciplinary board, the physician appealed to the Supreme Court of Washington.

The medical disciplinary board was established by the state legislature in 1955. It was given broad powers to discipline members of the medical profession for unprofessional conduct. It may reprimand a doctor or may suspend or revoke his license. Unprofessional conduct is defined as "Conviction in any court of any offense involving moral turpitude, in which case the record of such conviction shall be conclusive evidence." On May 4, 1956, the petitioner entered a plea of guiltv in a U. S. District Court to a charge of willfully attempting to evade a portion of his proper income taxes for the calendar year, 1949, by filing a false and fraudulent return. In August, 1957, the medical disciplinary board notified the petitioner that it would hold a hearing to determine whether or not his license to practice medicine should be revoked. In its specification of charges the board set out the above-mentioned conviction of tax evasion and charged that the offense involved moral turpitude and that it constituted unprofessional conduct within the meaning of the medical disciplinary act. The petitioner admitted pleading guilty to the federal offense but denied that the offense involved moral turpitude or constituted unprofessional conduct.

In our opinion, said the Supreme Court, a willful and intentional attempt to avoid payment of all or a part of one's income tax with intent to defraud the government involves moral turpitude. Such fraud is unprofessional conduct as that term is defined in the medical disciplinary act.

The daily practice of medicine, the court continued, concerns life and death consequences to members of the public. They have an understandable interest in the maintenance of sound standards of conduct by medical practitioners. The public has a right to expect the highest degree of trustworthiness of the members of the medical profession. We believe there is a rational connection between income tax fraud and one's fitness of character or trustworthiness to practice medicine, so that the legislature can properly make fraudulent conduct in such instances a ground for revoking or suspending the license of a doctor.

There was some doubt in the court's mind as to whether or not fraud (moral turpitude) inheres in every violation of the internal revenue law. There was not doubt, however, that fraud must be proved when the method of defeating or evading tax alleged in an indictment is by the filing of a false and fraudulent return. Since the method of tax evasion charged in the indictment of the petitioner was that of filing false and fraudulent returns and since he pleaded guilty to that charge, the court held that the issue of fraud (moral turpitude) was determined conclusively.

The judgment of the trial court affirming the revocation of the petitioner's license to practice medicine was therefore affirmed. *In re Kindischi,* 319 P(2) 824 (Wash. 1958).

Governmental Hospitals: Immunity from Tort Liability.—The plaintiff filed suit for damages because of injuries resulting from the alleged negligence of one of the nurses employed by the defendant hospital. From a judgment for the hospital, the plaintiff appealed to the court of appeals of Tennessee.

The plaintiff entered the defendant hospital as a paying patient in an obstetric case. She had been in the delivery room but was returned to her own room because her time had not yet come. While there, a student nurse, at the instruction of the registered nurse on the obstetric floor, gave the plaintiff an injection of Ergotrate, which was not supposed to be given until after delivery. The nurses assumed she had been delivered and failed to observe her condition which, said the court, should have been apparent. The administration of the drug caused the uterus to contract and this brought on pain and suffering and caused the infant to die of anoxemia.

The trial court held that the defendant was a governmental hospital and was, therefore, not responsible for negligent acts committed by its employees. It is clear, said the court of appeals, that the hospital was operated not for profit but at a loss to the city and county. The fact that about 87% of its operating cost was derived from private pay patients and the operation of such services as vending machines and tea rooms does not deprive it of its character or take away its immunity. It was maintained as a governmental function. The rule of governmental immunity, said the court of appeals, is well established in Tennessee and can only be overruled by the Supreme Court or taken away by the legislature. The court added that the immunity could be waived by the procurement of insurance. The insurance purchased by this defendant, however, did not cover or contemplate the covering of malpractice actions. It therefore did not amount to a waiver of immunity by the hospital.

The judgment in favor of the hospital was affirmed. *McMahon v. Baroness Erlanger Hospital,* 306 S.W. (2) 41 (Tenn., 1957).

Malpractice: Statute of Limitations Applicable.—This was an action for damages by a father on behalf of his minor child for injuries caused by the alleged malpractice of the defendant physician. From a judgment in favor of the defendant, the plaintiff appealed to the Supreme Court of Florida.

The issue involved in this case related to the defense of the statute of limitations. The Florida law provides a limitation period of three years for "an action upon a contract, obligation or liability not founded upon an instrument of writing" and a limitation period of four years for "any action for relief not specifically provided for in this chapter." No specific provisions of the law set forth definite periods of limitations for certain actions, including those for "personal injury," "injuries to the person," and malpractice suits against physicians.

The defendant contended that a malpractice action arises out of an implied contract and that actions thereon are limited by the three-year statute. The plaintiff, on the other hand, contended that a malpractice action sounds basically in tort and that, since there is no specific statute relating to tort or malpractice actions, it is an action "not specifically provided for" and is therefore governed by the four-year statute.

The Supreme Court said that there can be no doubt that where a transaction complained of has its origin in a contract and, at the same time, a duty is superimposed by or arises out of the circumstances of the transaction, the violation of which constitutes a tort, then the injured party has an election to sue in tort or for the breach of contract. Since, in this state, no special limitation period is provided for malpractice actions, there is no valid reason for applying to malpractice suits a rule different from the one applicable to other causes of action in which the plantiff has an election to sue in contract or in tort. In other words, the statutory period applicable to a malpractice suit depends upon the claim for relief stated by plaintiff—whether he sues for and seeks the damages applicable to a breach of contract or a tort.

In this case, said the court, both the original and the amended complaints filed on behalf of the minor plaintiff clearly stated a cause of action sounding in tort, although in the original complaint the employment of the plantiff was disclosed as a matter of inducement. Inasmuch as the complaint was filed within the four-year period applicable to tort actions, the judgment of the trial court in favor of the physician was in error. Accordingly that holding was reversed and the case was remanded for a trial on the merits. *Manning v. Serrano,* 97 So. (2) 688.

MISCELLANY

SOME GENERAL OBSERVATIONS ON MEDICAL AND PHARMACEUTICAL RESEARCH IN THE SOVIET UNION

C. Wesler Scull, Ph.D., Maurice Nance, M.D., Francis Grant
and
G. Fred Roll, Philadelphia

More than two years ago, Smith, Kline & French Laboratories, with the approval of the U. S. Department of State, initiated a series of discussions with diplomatic representatives of the Union of Soviet Socialist Republics designed to exchange scientific and administrative personnel. It was our belief that such an exchange would, at the very least, expand the horizons of our Research and Development Division. Earlier this year, we, together with Dr. W. Horsley Gantt, Associate Professor of Psychiatry, Johns Hopkins University, and Director, Pavlovian Laboratory of the Phipps Psychiatric Clinic, Johns Hopkins Hospital, constituted the first official United States pharmaceutical delegation to the Soviet Union. We visited medical and pharmaceutical research operations in Moscow, Leningrad, and Kharkov as the guests of the Russian government. Subsequently, five representatives of Soviet medical and pharmaceutical research—constituting the first such delegation from the Soviet Union to the United States—visited laboratories in the United States as our guests.

This is our delegation's first published report, and it is based on our visit of approximately 30 days in the Soviet Union and the U. S. S. R. delegation's stay in the United States of the same duration.

Perhaps the strongest impression that has come out of this exchange is that of the vitality of fundamental biological research in Russia. It is our feeling that the Soviet Union is making a determined effort to bring its biological research programs up to the level of its programs in the physical sciences. It is our observation also that current Soviet research in many areas of medicine equals the West's qualitatively, although it appears to lag behind the West's quantitatively.

The importance of Western research to Soviet programs is obvious from the speed with which publications from the West are received, trans-

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Director of Development (Dr. Scull), and Director of Cinical Investigations (Dr. Nance), Research and Development Division; Director, Research and Development Agreements (Mr. Grant); and Manager, Department of Public Relations (Mr. Roll); Smith, Kline & French Laboratories.

lated, and distributed. We saw journals, bulletins, and books which were only a month or two old, including state and local medical society bulletins. In one research center, entire issues of THE JOURNAL of the American Medical Association, minus advertisements, were reproduced and distributed. Some of the scientists we met could speak English, but an amazingly large proportion could read English; indeed, one scientist remarked to us that there were "only two important scientific languages now—English and Russian."

Therapeutic Preparations

From this emphasis on keeping up with Western research through the literature, it should come as no surprise that Soviet physicians have many of the same major therapeutic agents at hand as their Western colleagues. For example, they have the antibiotics, such as penicillin and the tetracyclines, and the sulfonamides. They employ many of the anesthetics which are in general use in the United States. (Because local and regional anesthesia is given preference over general anesthesia, the procaines seem to be in greater demand there than here.) And the Russians have a few of the phenotropic compounds, notably, chlorpromazine.

Such therapeutic agents are available with about the same "prescription-only" restrictions as in the United States. One notable exception is orally given penicillin, which is widely sold without restrictions. But officials in Russia, disturbed over the problems associated with indiscriminate use of penicillin, are considering withdrawing it as an "over-the-counter" item.

The number of ready-made proprietary preparations, of course, is far less than in the United States. Pharmacists, we were told, receive sufficient education to make simple diagnoses and to suggest proprietary remedies. The only pharmacies are state-operated and they are extremely busy. In Leningrad we saw 16 pharmacists in one establishment busily compounding prescriptions at the unlikely hour of 11:30 p. m.

An indication of the scope of the Soviet pharmaceutical industry can be gained from these figures, which, we believe, have never before been made available outside the U. S. S. R. In 1956, there were 12,951 pharmacies in the Soviet Union; 5,926 were in cities and the remainder in rural locations. This compares with some 52,500 United States operations which could be classified as pharmacies. However, the Soviet Union had a total of 128,353 pharmacists in 1956, compared with 110,567 in the United States. The value of "retail sales" of pharmaceutical products in the Soviet Union in 1956 was 417,270,000 rubles.

The observation about the number of packaged proprietary preparations applies also for the number of specialities which are available in a given class of compounds. The Soviet pharmaceutical industry, which, of course, is entirely controlled and directed by the Ministry of Health, will not market a range of compounds when one "standard" compound can be made to do. We were told by officials that, given the choice between production of a given agent in quantity or refinements either in product form or in the range of compounds, the Ministry of Health invariably would choose quantity. For example, although Soviet medical workers are entirely familiar with the newer corticosteroids, only cortisone and hydrocortisone have been made generally available. The same applies to phenotropic agents; at present only chlorpromazine and rauwolfia compounds are available, although other agents —newer phenothiazine compounds and meprobamate—are under clinical study.

Considering the fact that the Soviet state is attempting with limited production facilities to provide comprehensive medical programs for a vast population, the official stand on quantity versus multiple variants of compounds is by no means surprising. Production equipment is rough and ready, but adequate; it is scarcely comparable, however, to the highly automated stainless steel equipment we in the United States are accustomed to. Some of the machines appear to have been designed and built in Eastern Europe. In general, product forms could be compared to what was produced in the United States in the 1930's and early 1940's and are not up to the "finish" found currently throughout much of Western Europe. In our visits to pharmaceutical research and manufacturing facilities, we were told repeatedly that much thought and planning is under way to obtain more modern equipment within the next three to five years.

When a new agent is cleared for production, the Ministry of Health informs the medical profession and the public virtually simultaneously. Simple one-page "flyers" are sent to physicians giving the trade name, chemical name (using Latin nomenclature) and structure, indications, contraindications, side-effects, dosage range, and available dosage forms. But, at nearly the same time, the public is informed of the new agent via press and television.

The prime objectives of Soviet medical research are identical with those of the West: cancer and cardiovascular disease. The scope and kinds of investigations are generally similar to those in the United States. The programs in fundamental biolog-

Top (left), ampul packaging department of Leningrad's pharmaceutical plant no. 1, founded in the early 18th century by order of Peter the Great. This plant employs more than 1,000 workers. *Top (right),* medicinal plants collected from all sections of the Soviet Union being inspected by Drs. Gantt (*left*) and Nance (*third from left*). *Center (left),* visiting Americans observing finishing line techniques at a Russian pharmaceutical plant. *Center (right),* visitors and hosts gathered around bust of Pavlov at Pavlov Institute near Leningrad: *front row (left to right)*– Mr. Grant; Alexander G. Natradze, chemical engineer, member of Committee of Public Health, and Director of Pharmaceutical Industries in U. S. S. R.; E. C. Airapetianz, professor of physiology at the Institute; Dr. Scull; and Professor Tsubkalo; *second row (left to right)*–Deputy Director Soloviev, of the Institute; Dr. Nance; and Dr. Gantt. On the left of the Pavlov bust is Mr. Roll. *Bottom (left),* members of Russian team who toured Smith, Kline & French Laboratories visiting Philadelphia Museum of Art *(left to right):* Mariya Dmitriyevna Ushakova, physician and biochemist and member of the Institute of Antibiotics; A. G. Natradze; Prof. G. N. Perschin, Deputy Director of All Union Scientific Research Chemical-Pharmaceutical Institute, Moscow; S. P. Smiriensky, chief of planning department, Institute of Medical Industry; and D. K. Skolaban, chief engineer of Moscow District Medical Production, Ministry of Public Health. *Bottom (right),* A. G. Natradze *(left)* and G. N. Perschin *(right)* receiving their first impressions of Liberty Bell in Philadelphia.

ical research are strongly developed and well supported, but we found this to be less true for Soviet pharmaceutical research.

In the field of medicinal chemistry, Russian synthesis of compounds is qualitatively equal to that of Western work. Quantitatively, however, the Russians are considerably behind the West. It is our observation that, whereas in the West a single medicinal chemistry laboratory may synthesize 50 or 100 compounds for evaluation to find the optimal therapeutic agent, a comparable Russian pharmaceutical research institute will synthesize only 5 or 10.

Pavlovian Methodology

The most striking difference between fundamental biological research in the West and in Russia is that, in the U. S. S. R., one name and one approach finds its way into virtually every research protocol—Ivan Pavlov and the conditioned response. The Pavlov Institute near Leningrad has virtually achieved the status of a national shrine of science. The rooms Pavlov occupied are kept up as faithfully as they were on the day of the Nobel laureate's death in 1936.

Western science grants that Pavlov contributed significantly to psychology and physiology. But many Western scientists—indeed, the majority of them—feel that Russian science gives too much emphasis to his work.

Yet a much different impression of the value of Pavlovian methodology is gained when one is given the opportunity to investigate, at first hand, the rationale behind the U. S. S. R.'s emphasis on Pavlov. To begin with, the Russians are far more eclectic than would at first appear. Pavlov does permeate Russian medical research, but this orientation is rather like the West's toward the fundamental biological doctrines of such medical thinkers as Bernard and Cannon. At the same time—and this is the point to be made concerning the Russians' eclecticism—their scientists are far more familiar with Bernard and Cannon than Western scientists are with the methods, data, and philosophy of Pavlov and his successors. Thus, emphasis on Pavlov is not mere adulation for a hero of science.

In the United States we too frequently associate Pavlovian theory only with conditioning involving gross motor responses. We neglect the huge corpus involving visceral response and changes because, to our thinking, this material seems "foreign." But, although the West may choose to disagree with Soviet emphasis on Pavlovian theory, it is wrong for the West to ignore the immense amount of data obtained by Russian scientific workers who incorporate Pavlovian teachings in their research approaches. This body of experimental findings ranges from significant work in man and the primates down through the orders of life to the bee and the worm. Some of the experiments may seem bizarre, but they should not be disregarded on this basis.

One experiment involving the production of hypertension in primates is an amusing example of the ingeniousness of research done in Russia with use of an extension of Pavlovian technique. A male and a female ape are mated. Subsequently, the male is removed to an adjacent cage and a younger, more virile male is put in with the female. The first male is obliged to look on as his former mate enjoys the affections of the interloper. The "emotional" strain on the deprived male produces hypertension.

A second experiment with primates involves mother and offspring. The mother is dressed in a blanket every time the child is placed with her for feeding. Soon the offspring associates "mothering" with the blanket and not the mother and is thus literally weaned away from the mother and "weaned to" the blanket.

If only because of the ability of Soviet scientists to produce, as in the first example, physiological states by other than the usual physiological means, Western science owes it to itself to pay more attention to Russian experimentation. And, as in the second experiment, with its "Brave New World" overtones, the West cannot afford to ignore work which produces behavior of a higher order than mere motor reactions to a light or buzzer with noxious stimuli.

Summary

The Soviet Union and the West have common research goals. The U. S. S. R. is entirely familiar with Western methodology and uses this methodology together with its own experimental approaches based on the work of Pavlov. Every class of therapeutic compounds developed by the West is in clinical use in Russia. A new emphasis apparently has been placed on fundamental biological research, and, although Soviet medical science lags quantitatively behind Western science, qualitatively the work is comparable. Having been given the opportunity to see this experimental work at first hand, it is our suggestion that the West pay more attention to the data and methods of Russian biological science.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Critical Consideration of Therapy of Myocardial Infarct. O. Bayer, H. Maring and J. M. Schmitt-Rohde. Deutsche med. Wchnschr. 83:792-796 (May 2) 1958 (In German) [Stuttgart, Germany].

Vascular wall changes of a degenerative or inflammatory nature, slowing-down or obstructive retardation of the blood flow, and changes in the coagulation process are factors in the development of thrombosis. More attention has been given to the relationship between the mechanism of coagulation and the circulatory function since the American Heart Association in 1948 recommended the use of anticoagulants in the treatment of cardiac infarcts, but the importance of the rate of flow deserves more attention in the treatment of cardiac infarct and in the prevention of its complications than has been the case so far. A coronary thrombosis with the consecutive development of a myocardial infarct frequently leads by way of a reflex mechanism to a complicated acute circulatory reaction, a shock syndrome. There is a sudden reduction in the peripheral circulatory resistance, usually combined with a reduction in the beat and minute volumes, and this is followed by a decrease in the arterial pressure in the systemic circulation with the symptoms of collapse. The resulting pressure fall in the coronary circulation reduces the speed of the blood current, and this, in turn, favors the growth of the thrombus and causes obstruction of additional vascular branches. These factors emphasize the importance of an optimal blood flow speed through the coronary vessels.

The authors review observations on 350 patients with clinically demonstrated heart infarcts. The number of infarct relapses and of thromboembolic complications was greatest in the patients who either had a critical reduction of the arterial pressure, or in whom the coagulation potential had not been reduced by the administration of anticoagulants. The largest majority of the patients who died had experienced prolonged periods of collapse. The authors present the histories of 2 patients, which illustrate the great importance of circulatory factors in cardiac infarct. The first patient, who died, had had prolonged cardiac insufficiency for which no proper treatment had been given. In the second patient, the collapse had been counteracted promptly with the aid of arterenol drip infusion and other measures, and this patient recovered. Restoration and maintenance of adequate blood pressure and suitable reduction of the coagulation potential are stressed as vital factors in the treatment of cardiac infarct.

Stokes-Adams Attacks Treated with Corticotrophin. J. W. Litchfield, K. A. Manley and A. Polak. Lancet 1:935-937 (May 3) 1958 [London].

At present only adrenergic substances and atropine are used in the treatment of Stokes-Adams attacks, and they often have no effect on the condition. The authors report sustained improvement after the use of corticotropin in 3 patients with Stokes-Adams attacks which did not respond to conventional treatment. The frequency and severity of Stokes-Adams attacks may change unpredictably even in the untreated patient, and spontaneous remissions are known to occur. The success of any treatment is therefore difficult to establish. The authors consider it unlikely that the improvement which followed corticotropin therapy was due to chance in any of the following cases: In case 1 an unstable cardiac rhythm of at least six weeks' standing was converted to a stable rhythm within 6 days of the first injection. In case 2 attacks which had occurred with a frequency of 1 to 40 a day for many weeks stopped within a few hours of the first injection and recurred twice when the dose was reduced. The attacks of syncope in case 3 were far less numerous but had been occurring for 8 weeks, and electrocardiography during the last 12 days had consistently shown grossly abnormal conduction. The attacks ceased within 6 hours of the first injection, and the electrocardiogram rapidly returned to normal.

The authors mention several previous reports in which either corticotropin or cortisone was used successfully in similar cases. They used corticotropin in the 3 patients because it seemed possible that the heart block was due to inflammation of the bundle of His. The first patient had ankylosing spondylitis, a disease in which carditis is known to

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The place of publication of the periodicals appears in brackets preceding each abstract.

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occur. In the second patient the presence of aortic stenosis of rheumatic origin suggested that the bundle might be damaged by a rheumatic lesion. In the third patient the origin of the heart block was more obscure, but malaise, herpes simplex, and raised erythrocyte sedimentation rate all pointed to infection as an underlying cause.

Polycythemia with Papilledema and Infratentorial Vascular Tumors. G. F. Starr, C. F. Stroebel and T. P. Kearns. Ann. Int. Med. 48:978-986 (May) 1958 [Lancaster, Pa.].

Of 106 patients with infratentorial vascular tumors who were operated on at the Mayo Clinic, 38 (36%) had hemoglobin values greater than 15 Gm. per 100 cc. of blood. Eleven of these patients had hemoglobin values greater than 18 Gm. per 100 cc.; 10 of these had papilledema. The vascular tumors in these patients were of the hemangioendothelioma type, and both cystic and solid tumors were observed. In patients with increased hemoglobin level and papilledema, the possibility of a vascular tumor in the posterior fossa must be excluded before the papilledema is attributed to polycythemia alone. The incidence of absolute polycythemia secondary to cerebellar vascular tumors must be relatively rare. Four of the 11 patients had blood volume determinations; of these, 1 had absolute secondary polycythemia, 1 had a borderline absolute secondary polycythemia, and 2 had relative polycythemia. The mechanism of production of polycythemia in patients with these tumors is not known. That such an association exists is supported by the fact that the hematological findings became normal in 6 of the 11 patients after operation. Three of the remaining patients died in the immediate postoperative period, and data were, therefore, not available. A similar return to normal of the hemoglobin level and of the erythrocyte count occurred in 15 of the 26 patients whose cases were collected from the literature. The necessity of studies of blood volume in the accurate documentation of these cases is stressed, since infratentorial vascular tumors are an adequate cause of relative polycythemia.

Acute Rheumatic Fever: A Study of 132 Cases in Young Adults. R. C. Bates. Ann. Int. Med. 48:1017-1025 (May) 1958 [Lancaster, Pa.].

The author reports the clinical manifestations of acute rheumatic fever in 132 men, between the ages of 17 and 28 years, in military service who were treated at the naval hospital in Great Lakes, Ill., between 1944 and 1956. The patients, on admission, were placed in bed and were given 300,000 units of procaine penicillin G intramuscularly, daily for 10 days, to eliminate streptococci. Aspirin in divided doses totaling 6 Gm. daily was given for the first 2 days, and 4 Gm. daily thereafter. Patients with carditis were given cortisone, in addition to aspirin, in a dose of 300 mg. the first day and 200 mg. daily thereafter until all manifestations apparent at the bedside had subsided; the dose, then, was gradually reduced over the next 3 or 4 weeks. Notable was the complete absence of chorea, heart failure, cardiac enlargement, or deaths. In contrast to patients with rheumatic fever reported on by other workers, all these patients had objective arthritis at some time during their course. Other manifestations of rheumatic fever were anemia in 24 (18.2%), albuminuria in 11 (8.3%), pulmonary infiltration in 4, abdominal pain in 3, and a pericardial rub in 1. Petechiae occurred in 6, erythema nodosum in 2, and herpes simplex in 1. The most significant association of persistence of organic heart murmurs was that with fever. Persistent organic murmurs necessitating discharge from military service occurred in 37 patients (28%). One hundred four patients (78.8%) were hospitalized for less than 60 days until they were able to return to full duty.

Prompt diagnosis and hospitalization, with early abolition of streptococci by the administration of penicillin, resulted in a more benign course of the disease and a shorter period of disability but did not materially reduce the incidence of valvulitis. Attempts to identify features of the illness that accompany valvulitis were unrewarding, and valvulitis was found to be an early feature of the disease in most cases. These observations suggest that valvulitis may be entirely separate from all other clinical features of rheumatic fever and may not be entirely prevented by any currently known method of therapy. No evidence was found that rest in bed beyond the period of acute carditis is of any value in determining the final outcome, or that prolonged rheumatic activity leads to greater heart damage in patients in this age group.

Musculoskeletal Manifestations of Systemic Lupus Erythematosus, Polyarteritis Nodosa, Dermatomyositis and Diffuse Scleroderma. W. M. Mikkelsen, H. A. Zevely, N. H. Chatelin and I. F. Duff. J. Michigan M. Soc. 57:715-721 (May) 1958 [St. Paul].

The authors report on 50 patients with collagen or connective tissue disease who died at the University of Michigan Hospital in Ann Arbor, and on whom autopsies were performed. Of these, 21 had systemic lupus erythematosus, 18 had polyarteritis nodosa, 5 had dermatomyositis, and 6 had diffuse scleroderma, as confirmed by autopsy. In these patients, musculoskeletal manifestations occurred commonly and frequently, which resulted in confusion with rheumatoid arthritis and rheumatic fever. Musculoskeletal symptoms were the initial manifestation in 8 (38%) of the 21 patients with lupus erythematosus and occurred ultimately in 18 (86%) of this group. Arthralgia and/or myalgia was unaccompanied by objective joint findings in 7 patients (33%). Objective evidence of synovitis was observed in 11 patients (52%). Physical findings in regard to the joints were sufficiently severe and persistent in 5 of these patients to suggest rheumatoid arthritis, while the migratory pattern of joint involvement was suggestive of rheumatic fever in 4. The correct diagnosis was usually suggested by one or more of the following findings: discrepancy between the severity or course of articular and extra-articular manifestations; erythematous eruptions of the face; serous membrane involvement with effusion; evidence of renal impairment; convulsions; toxic psychoses; clinical evidence of cardiac disease; false-positive reactions of the patients' blood to serologic tests for syphilis; leukopenia; and presence of L. E. cells.

Musculoskeletal manifestations represented the mode of onset in 4 (22%) of the 18 patients with polyarteritis nodosa. Although such symptoms were noted at some time in 10 patients (55%), in only 4 (22%) were objective changes in the joints described, which caused confusion with rheumatoid arthritis in 2 and with rheumatic fever in the other 2. The diagnosis of polyarteritis nodosa should be suspected when eosinophilia in excess of 25% develops in a patient with bronchial asthma or when marked systemic or other symptoms, not readily explained on the basis of the original diagnosis, occur in a patient with hypertensive renal disease or apparent rheumatoid arthritis. The following signs and symptoms occurred with some frequency in this group of 18 patients and should also suggest the diagnosis: peripheral neuritis; abdominal pain; peptic ulcer; unexplained gastrointestinal bleeding; hypertension; nodular or necrotizing skin lesions; abnormal urinary findings; intermittent testicular pain; Loeffler's syndrome; roentgenologic evidence of diffuse granular disease of the lung; persistent unexplained polymorphonuclear leukocytosis; or a recent history of serum sickness or reaction to sulfonamide compounds or penicillin.

Subjective musculoskeletal involvement occurred in 3 (60%) of 5 patients with dermatomyositis. Although flexion contractures occurred in 2, differentiation from rheumatoid arthritis was possible because of the absence of the usual physical signs of inflammatory intra-articular disease. As the disease progressed in these patients, muscular atrophy and weakness eventually far exceeded that observed in the other patients of this series. All 6 patients with diffuse scleroderma had musculoskeletal complaints; in 5 (83%) these represented the mode of onset. Although some degree of flexion deformity occurred in all the patients, differentiation from rheumatoid arthritis was again made possible by lack of evidence of inflammatory involvement of joints. The possibility of a connective tissue disease, and particularly of systemic lupus erythematosus, should be considered in patients with apparent rheumatoid arthritis, whose cases are atypical or associated with multiple system involvement.

Carcinoma and Ulcerative Colitis: A Clinical and Pathologic Study: I. Cancer Deaths. M. B. Goldgraber, E. M. Humphreys, J. B. Kirsner and W. L. Palmer. Gastroenterology 34:809-839 (May) 1958 [Baltimore].

This paper is a report on 14 patients, of whom 12 died of colonic cancer and 2 of rectal carcinoma, among a total of 86 patients who died from various causes. On the basis of these 14 patients, carcinoma of the large intestine complicating chronic ulcerative colitis appears to have the following characteristics: 1. It occurs at an earlier age than "ordinary" colonic cancer. 2. It arises after an average duration of symptoms of ulcerative colitis of 17 years. 3. It has a tendency to a more diffuse distribution throughout the colon. 4. It often presents a linitis plastica type of lesion and a multiplicity of sites of origin. Because of the underlying disease there are difficulties, both clinically and roentgenologically, in the diagnosis of the carcinoma. The rectosigmoid stump left behind after colectomy was the site of cancer in 2 patients. The carcinoma may arise in an atrophic as well as in a hyperplastic type of mucosa.

A Mild Form of Leptospirosis Due to Leptospira Canicola: Report of 3 Cases in Children. M. Yow and A. Megarity. Texas J. Med. 54:308-312 (May) 1958 [Austin].

The authors report 3 children in whom leptospirosis was diagnosed in Houston during the past year. Two were 13-year-old boys, and 1 was a 5-year-old boy. The infections were mild and were traced to Leptospira canicola by agglutination lysis tests. The infections presented as aseptic meningitis in 2 patients and fever of unknown origin in the third. The most striking manifestations in these patients were fever, extreme myalgia, gastrointestinal upset, and central nervous system involvement. The myalgia in all 3 was most marked in the lower extremities. The signs of central nervous system involvement varied from nuchal rigidity to mental confusion. Two patients had skin lesions of maculopapular or morbilliform type. None of these children was jaundiced, and bilirubin determinations on 2 of them were within normal limits. Antibiotic therapy did not appear to alter the course of the disease, and the duration of illness was 7 days in 1 case and 10 days in the other 2. There were no sequelae in 2 patients, and there was no follow-up on the third. Two of the children had dogs for pets; however, the animals were not available for study.

Leptospiral disease due to Leptospira canicola is not considered a common disease in Texas, but the circumstances exist for human infection, since leptospiral disease in the dog is frequently reported in this area. The milder forms of human leptospirosis may be misdiagnosed because of their variable symptomatology. Serodiagnostic tests for this disease are available, and emphasis should be placed on their use in the differential diagnosis of benign aseptic meningitis, infectious hepatitis, and fever of unknown origin. There is no specific treatment for leptospirosis. Prevention of leptospiral infection in the animal host offers the most practical approach to the problem in man. The organism is excreted in the urine of the infected dog during the disease and for as long as 6 months after the active disease. Man acquires the infection by intimate contact with the animal host or by contact with damp soil or water contaminated with infected excreta. The only known route of human infection is through abrasions in the skin or through intact mucous membranes of the eye and nasopharynx.

Vascular Disease in Diabetes Mellitus: The Importance of the Obesity Factor. A. J. M. Campbell. Scottish M. J. 3:199-204 (May) 1958 [Glasgow].

The author investigated the incidence of vascular lesions in diabetic patients, with special reference to the possible etiological significance of coexistent obesity. The investigation was focused on diabetic retinopathy and degenerative heart disease, these being considered as representative of the 2 types of vascular disease, specific and nonspecific, potentially present in any diabetic patient. Two groups of persons, all 40 years of age and older, were investigated. The first group consisted of diabetic patients selected at random from those attending a diabetic clinic. There were 156 such patients, 116 women and 40 men. They were divided into those who were 6% or more above average weight (the overweight group) and those of average normal or subnormal weight. There were 81 in the former and 76 in the latter group. A control group, numbering 162—104 women and 58 men—similar in age to the diabetic group, was selected to obtain a cross section of the general population.

A total of 30 diabetic patients, 24 women and 6 men, were found to have retinopathy. While there was no definite correlation between the patient's age and the frequency of this lesion, the incidence of the retinopathy did increase with the duration of the diabetes both in women and in men. Whereas diabetic retinal lesions were found in 10.8% of those who had had diabetes for less than 5 years, it was found in 34.4% of those who had had diabetes longer. The weight of the patient, however, did not significantly influence the development of retinopathy. Of the 81 overweight patients, 20.9% had retinal lesions, and of the remaining 76 patients, normal or below normal in weight, 17.1% had retinal lesions.

To ascertain the presence of degenerative heart disease, electrocardiographic records were obtained in both diabetic and control groups of patients. A total of 63.7% (97) of the diabetic patients, compared with 35.8% (58) of the control subjects, were found to have abnormal tracings. This excess of abnormal electrocardiograms in the diabetic series is statistically significant. In both groups there was a steady rise with age, but the diabetics showed a higher incidence in each decade. It is believed that significant reduction in cardiovascular morbidity and mortality can be achieved by weight reduction in overweight diabetic patients.

Atypical Manifestations of Gout. E. Coodley. California Med. 88:375-379 (May) 1958 [San Francisco].

Because the classic picture of gouty arthritis is so well known, there is danger of missing the diagnosis in atypical cases of this disease. The author presents the history of 5 patients with an atypical form of gout. The first patient was a 37-year-old woman who complained of painful swelling of both hands, recurring every few weeks and lasting several days each time. These symptoms had been present for 5 years. There had been 1 episode of swelling of the left foot 3 years before, but never any involvement of the big toe of either foot. The only significant laboratory finding was the serum uric acid concentration, 6.6 mg. per 100 cc. Roentgen-ray studies showed multiple cyst-like rarefactions at the metacarpophalangeal joints and also at the metatarsophalangeal joints. The patient was treated with colchicine orally at the next attack, with prompt relief of symptoms. The second patient, a 64-year-old woman, had nodular swelling, slight tenderness, and moderate limitation of motion in both hands. Both elbows had subcutaneous subolecranon nodules. In the right ear lobe a small, firm, nontender nodule was palpated. Serum uric acid content was 7.7 mg. per 100 cc.

The third patient, a 11-year-old girl, had pain and swelling in the left first metatarsophalangeal joint, lasting several days, then spontaneously disappearing but recurring several months later. An aunt and an uncle of the patient had had gout. The plasma uric acid content was 7.7 mg. per 100 cc. A 52-year-old woman had acute painful swelling of the right wrist, which had persisted 4 days, with redness, local tenderness, and limitation of motion by pain; a similar episode had occurred several months before. This patient, like the 5th one, a 32-year-old man, subject to periodic swelling of both ankles and once of the large toe, had elevated plasma uric acid levels. In this last patient the differentiation of episodic rheumatoid arthritis from gouty arthritis proved difficult. Increase in uric acid, response to therapy, and a negative result on hemagglutination test made the diagnosis of gouty arthritis more probable.

The Present Status of the Treatment of Chronic Ulcerative Colitis with Steroid Hormones. B. D. Rosenak, R. D. Pickett, H. D. Van Vactor and others. Gastroenterology 34:879-891 (May) 1958 [Baltimore].

The authors report the results of treatment with corticotropin and the steroid hormones given to 60 patients with ulcerative colitis. There were 35 acute cases, 20 of which represented primary or initial attacks and 15 acute exacerbations of preexisting disease. Of the 25 chronic cases, 11 were considered to be severe and 14 to be of moderate severity. The criteria for this classification consisted primarily of the degree of fever, number and frequency of stools, weight loss, bleeding from the intestine, and other clinical signs. Corticotropin alone was used in treating 10 patients, but most of the patients were treated initially with corticotropin in doses of from 20 to 40 mg. of aqueous corticotropin given intravenously in 500 to 1,000 cc. of 5% glucose in distilled water over a period of 6 to 10 hours, or 25 to 50 mg. given intramuscularly at 6-hour intervals for from 4 to 14 days, after which the patients were given maintenance doses of cortisone (25 mg., 1 to 4 times daily) or prednisone (2.5 to 5 mg., 1 to 4 times daily). Thirty patients were treated in this manner for periods ranging from 14 to 455 days. Only 5 patients were treated with prednisone alone. These patients were started on 30 to 40 mg. in 3 or 4 equal doses daily for from 2 to 5 days, and the dosage was then gradually reduced to from 5 to 15 mg. a day in divided doses.

Remission of the disease occurred in 32 of the 60 patients treated by these methods. Fifteen of the patients were somewhat improved, 6 remained unimproved, and 7 died (11.6%). The duration of the remissions lasted from 2 months to 4 years and averaged 17 months. Of the 35 patients in whom the disease was acute, 19 went into remission on treatment, with the duration of the asymptomatic state averaging 19 months. Thirteen of the 25 patients with chronic ulcerative colitis had remissions averaging 10 months in duration. Of the 32 patients who went into remission, 10 suffered a relapse within 6 months after termination of the hormone therapy, and another 10 relapsed after six months. Eleven of the 20 who relapsed responded to treatment with steroids, 7 did not respond, and 2 were not retreated. There was no relation between the type of hormone therapy used and the incidence of relapse.

At the time when treatment with steroid hormones was started, most of the patients were in a period of severe exacerbation of the disease with fever and severe diarrhea. A few had experienced moderate bleeding and several had developed anal complications; but none had perforation, giant ulceration, or massive hemorrhage before treatment. The most frequent complication, which consisted of involvement of the anus with abscess or fistula, was observed in 28% of the patients; this was higher than anticipated and may indicate aggravation resulting from hormone treatment. Hemorrhage, severe enough to cause symptoms of shock, was seen in 10 patients, or 17% of the total. Thus, the frequency of severe hemorrhage seems to be greater than usual in this disease. Acute manic psychoses considered to be attributable to the therapy occurred in 10 patients (17%), and depression occurred in an additional 12%. Giant ulceration of the colon was observed in 7 (12%). Perforation of the colon was observed in 7 (12%). Two complications which are associated with steroid therapy, namely, hypokalemia and adrenal insufficiency, were seen in 11 and 8 patients respectively. Peptic ulcer developed in 8 patients while they were on steroid therapy. Perforation occurred in 2 of these: 1 was operated on and recovered; 1 died and was found on postmortem examination to have multiple perforations of gastric and jejunal ulcers with peritonitis, which had not been recognized clinically. All 7 of the patients who died were acutely ill when hormone treatment was started. They were not benefited by these drugs, and in some way the use of the hormones complicated the course of the disease and may have hastened death.

The authors believe that the steroid preparations should not be used routinely in patients with chronic ulcerative colitis, but that they should be reserved for those (1) who have acute fulminating disease, (2) who are not improving on routine medical treatment, (3) who have complications, such as arthritis or uveitis, and (4) who must undergo surgical procedures, particularly if they have had a previous trial of hormone therapy. In such cases these agents may assume a primary role in treatment.

Malignant Lymphomas and Leukemias. D. S. Carroll. J. Louisiana M. Soc. 110:154-160 (May) 1958 [New Orleans].

The author differentiates the following groups of malignant lymphomas: (1) giant follicular lymphoma, (2) lymphosarcoma, (3) reticulum-cell sarcoma, and (4) Hodgkin's disease. Giant follicular lymphoma, or Brill-Symmers disease, differs from the other lymphomas in its slowness of growth, its tendency to remain quiescent for longer periods, and the frequency with which it appears as a solitary lesion. Retroperitoneal lymph nodes are commonly involved, and, unlike lymphosarcoma, involvement of the gastrointestinal tract or tonsils is infrequent. Because of the relatively benign course and slow development, the disease is frequently rather far-advanced when first seen. Histologically, there is a numerical and dimensional increase in the lymph-node follicles. The condition is radiation-sensitive, and the majority of patients live for 5 years. Survival for 10 years and even longer is not infrequent. In lymphosarcoma of the lymphocytic-cell type the predominant tumor cell is a small cell that is slightly larger than a small lymphocyte. The involved lymph nodes are replaced by yellowish gray homogenous cellular tumor. The architecture of the node is erased, and the tumor grows in the surrounding loose perinodal tissues. Lymphosarcoma exhibits great variation in the organs involved but is not necessarily a generalized disease. The primary lesion may be in the nasopharynx or in the tonsil, and, from a standpoint of treatment and prognosis, it may behave as a localized disease.

Reticulum-cell sarcoma may involve any tissue of the body, but it seems to involve bone more often than do the other types of malignant lymphoma. The characteristic cell is larger than the lymphocytic cell of lymphosarcoma. This tumor may appear as a solitary bone lesion, and in such cases the prognosis is relatively good. Hodgkin's disease is perhaps the commonest of the malignant lymphomas and is seen frequently in young adults. It is twice as common in men as in women. Clinically one can divide Hodgkin's disease in to 3 different forms: (1) a chronic form with slow development, in which the peripheral or purely lymphatic manifestations predominate; (2) an intermediate form, which includes about half of the cases, with faster development and early visceral manifestations; and (3) an acute form with early anemia, rapid weight loss, and early demise. The most frequent first symptom of Hodgkin's disease is a painless enlargement of a peripheral lymph node. Biopsy is essential to diagnosis. All forms of lymphoma respond to irradiation. Nitrogen mustard can be of great help, particularly in the patient with Hodgkin's disease.

Leukemia can be considered a malignant neoplastic disease of the hemopoietic organs, involving primarily the bone marrow and the lymphatic and reticuloendothelial systems. Essentially it consists of an acquired inability of immature leukocytes to respond to forces normally regulating their proliferation and maturation. The author considers the common chronic varieties of leukemia only, since acute leukemia is never successfully treated by radiation therapy. From his own experiences in the management of chronic leukemia, he stresses the following: 1. The least amount of radiation that will produce adequate relief of symptoms is the best dosage. 2. Retreatment should be instituted when the blood count just begins to increase, when anemia begins to become slightly more severe, when the basal metabolic rate begins to increase, or when the patient begins to show fatigue, anorexia, loss of weight, or bone pain. 3. Reliance should not be placed exclusively on irradiation; blood transfusions are of tremendous value, and iron therapy is often helpful.

Treatment of Lymphaic Leukemia and Other Malignant Leukoses with Radioactive Bismuth. J. T. van der Werff and C. A. M. Haanen. Nederl. tijdschr. geneesk. 102:625-630 (March 29) 1958 (In Dutch) [Amsterdam].

The therapeutic use of radioactive bismuth was first discussed at the second conference on radioisotopes at Oxford in 1954. Radioactive bismuth is a product of the cyclotron, not of the nuclear reactor. The atoms of the radioactive bismuth are not all identical, but the bismuth citrate in isotonic solution represents a mixture of the 4 radioactive isotopes, Bi^{204}, Bi^{205}, Bi^{206}, and Bi^{207}. These have different half-lives, but all 4 emit gamma rays. The chief component is Bi^{206} which accounts for about 80% of the radioactive energy. The citrate suspension of the radioactive bismuth is always mixed with a 5% suspension of active charcoal. After intravenous injection of the suspension, the charcoal particles, and with them the radioactive bismuth particles, are carried to the reticuloendothelial cells of liver, spleen, and lymph nodes.

The authors used radioactive bismuth and charcoal suspension in 84 patients with lymphatic leukemia and other forms of malignant reticuloses. Thirty-nine of these patients, for whom 8 or more months had elapsed since the radioactive bismuth therapy, were subjected to a thorough examination. It was demonstrated that healthy bone marrow is hardly affected by this treatment, and there were no signs of damage to liver or kidneys. A complete remission was obtained in all cases of lymphatic leukemia, except those which were in the final stage. Unexpected improvement or complete remission was also seen in a number of patients suffering from other malignant reticuloses. From these results it may be concluded that radioactive bismuth is a valuable aid to therapy.

SURGERY

Carotid Ligation for Intracranial Aneurysm: A Follow-Up Study of 54 Patients. W. G. Hardy, L. M. Thomas, J. E. Webster and E. S. Gurdjian. J. Neurosurg. 15:281-289 (May) 1958 [Springfield, Ill.].

The authors report the results of a 1-to-13-year follow-up study of 53 patients with intracranial aneurysm treated by ligation of the carotid artery in the neck, and of 1 patient with aneurysm of the internal carotid in the neck which was excised. Carotid ligation was a primary procedure and was not the result of a hemorrhagic complication occurring during an intracranial operation. Thirty-six of the aneurysms were in the distribution of the internal carotid and middle cerebral arteries; 7 were on the posterior communicating and posterior cerebral arteries; and 11 were in the distribution of the anterior cerebral artery. Four of the 54 patients became paralyzed postoperatively. The aneurysms were located distal to the internal carotid artery in 3 of these cases and on the internal carotid in 1 case. Seven patients have died. Three died of recurrent hemorrhage after ligation. Two of these had aneurysms on the circle of Willis; the third had multiple lesions of the internal carotid and anterior cerebral arteries. The patients with complication or repeated hemorrhage had aneurysms located predominantly distal to the internal carotid artery. Forty-two patients are working, and 3 are unable to work. Recurrent symptoms since ligation have been mild and infrequent. Although this is a selected group of cases, it appears that carotid ligation in the neck is of value in the treatment of intracranial aneurysms, particularly those of the internal carotid artery.

Results of Surgical Treatment of Intracranial Metastasis from Pulmonary Cancer: Report of a Case with Five-Year Survival. L. Bakay. J. Neurosurg. 15:338-341 (May) 1958 [Springfield, Ill.].

In the 10 years between 1945 and 1955, 64 patients with intracranial metastases of known primary site were operated on on the neurosurgical service of the Massachusetts General Hospital, Boston. A seemingly complete removal of the lesion was performed in 50 patients, partial resection in 8, and decompression alone in 6. The primary tumor was situated in the lung in 27 patients (42%). The survival of patients with metastasis from the lung was very short. Four patients, who had had previous pulmonary resection, did not fare better than those who had had no pulmonary surgery. About half of the entire group of patients died within 4 weeks, and all but 2 of the others in less than 6 months. One patient lived 10 months and was able to work for the first 7. Only 1 patient lived for 5 years, and his history is presented in detail.

The man, who was hospitalized in October, 1951, had been a heavy smoker and had a "cigarette" cough. Five weeks before admission he coughed up a small amount of blood. Marked papilledema was observed in both eyes. In spite of occasional unsteadiness and clumsiness of the left hand, he performed tests of coordination quite well. Films of the chest demonstrated a mass, about 5 cm. in diameter, surrounding the upper portion of the root of the left lung and radiating anteriorly and superiorly into the anterior and apical segments of the left upper lobe. Through the bronchoscope a papillary carcinoma was seen. Encephalography suggested that the patient might have 2 brain lesions. Ventriculography indicated a lesion in the right parietal lobe. Parietooccipital craniotomy was performed on the right side, and a walnut-sized solid tumor was removed from the parietal lobe. The tumor proved to be a metastatic papillary adenocarcinoma. The postoperative course was favorable. In December, 1951, some pain had developed over the left 5th rib. Roentgenograms of the chest revealed further progress of pneumonitis and further collapse of the left upper lobe. However, on bronchoscopy the tumor still looked resectable. Lobectomy was rejected, and roentgen-ray treatment to the lung lesion was decided upon, partly on account of the limited pulmonary function and because a metastasis had already been removed and there was some evidence suggesting another metastasis in the left temporal area. An estimated dose of 3,000 r was delivered to the left upper pulmonary lobe. The lung tumor resolved, leaving a lineal scar, which showed no change during the subsequent years. Hemoptysis ceased; the patient gained weight and looked well.

In March, 1956, however, the patient became blind and occasionally disoriented, and in the second half of 1956 he showed increasing signs of psychosis. He died on Jan. 27, 1957. At autopsy exploration of the bronchial tree revealed no evidence of tumor. Brain lesions included a cyst in the right cerebral hemisphere and a tumor in the left hemisphere. The author feels that the outlook for patients with cerebral metastasis from bronchopulmonary cancer is poor despite the fact that such a metastasis is not infrequently solitary. However, resection of the metastasis when situated in a nonvital part of the brain, followed by pulmonary resection or energetic radiation of the lung lesion, is indicated, because in occasional cases it can prolong useful life for a considerable length of time.

Chemopallidectomy and Chemothalamectomy. I. S. Cooper and G. Bravo. J. Neurosurg. 15:244-250 (May) 1958 [Springfield, Ill.].

The authors list criteria by which to judge a neurosurgical technique, the aim of which is to produce a lesion deep in the brain for the alleviation of hyperkinetic disorders. They feel that their method of chemopallidectomy via a convexity approach meets these demands. A pneumoencephalogram is performed prior to operation. A line (line C) is drawn on the scalp, which represents a plane 5 mm. behind the foramen of Monro. This line remains visible throughout the operation and serves as 1 of the 2 important external landmarks for orientation. A trephine opening is placed 5.5 cm. from the midline directly on line C. The chemopallidectomy guide is placed on the scalp and fixed so that the cannula holder is poised above the trephine opening on line C, thus insuring that the cannula will be introduced into the brain in a plane 5 mm. behind the foramen of Monro. The second external landmark is the inner canthus of the ipsilateral eye. The cannula is placed in the guide, and the top of the cannula is directed toward the inner canthus of the eye. The cannula is than pushed 2 cm. into the brain substance. At this point it is necessary to switch to the internal pneumoencephalographic landmarks. A lateral roentgenogram and an anteroposterior roentgenogram of the skull are developed on Polaroid film, so that the pictures become available in 50 seconds. When the cannula is aimed at the proper points, it may then be placed at its proper depth, which is at the level of the middle of the third ventricle. This is usually 6.5 cm. beneath the cortex. A balloon at the end of the double-lumen cannula is inflated by injection of Hypaque into the lumen leading to this balloon. This provides 2 functions: 1. It forms a cavity for later injection into the brain, thereby preventing any spread or reflux of the neurolytic agent. 2. It provides a physiological lesion in the globus, which temporarily alleviates contralateral tremor and rigidity when the cannula has been properly localized. The cannula is fixed in place, and the patient is returned to his room, allowing the cannula to remain indwelling in the brain for later gradual infliction of the lesion.

The series of alcohol or Etopalin injections are begun 24 to 48 hours after surgery. The intracerebral balloon is deflated, and the first alcohol injection is given. All injections are carried out with the patient in a sitting posture after the position of the cannula has been checked roentgenographically. Alcohol in doses of 0.5 to 0.7 cc. is injected 2 or 3 times over a period of 7 days. The neurolytic agent, alcohol, is mixed with iophendylate, so that the production of the lesion may be followed roentgenographically. The end-point is reached when the desired clinical result is achieved and when the roentgenographic appearance of the lesion seems adequate. If, 1 week after surgery, the symptoms are not adequately relieved, the patient is returned to the operating room, and a second cannula is placed by hand, usually approximately 7 to 13 mm. behind the first. A second lesion is then placed in the brain at this location, and almost invariably the summation effect of these 2 lesions will produce the desired result.

In their last 200 procedures the authors have placed the initial lesion in the thalamic location. This lesion is located slightly behind the midway point between the posterior margin of the foramen of Monro and the pineal gland. The use of this thalamic lesion is to be preferred to the pallidal lesion for relief of Parkinsonian tremor. Moreover, it is also effective in relieving rigidity. The authors performed more than 650 chemosurgical interventions for tremor and rigidity of Parkinsonism. They found that chemopallidectomy and/or chemothalamectomy in properly selected cases will provide lasting alleviation of tremor and rigidity in more than 80% of the cases of Parkinsonism. The mortality rate was 2.4%, and the incidence of lasting hemiplegia was 2%.

Clinical Aspects of Endangiitic Aortic Thromboses. G. Carstensen. Deutsche med. Wchnschr. 83:796-799 (May 2) 1958 (In German) [Stuttgart, Germany].

Endangiitic aortic thrombosis may originate on the vascular wall or as a sequel of an ascending thrombotic process on the basis of a unilateral or a bilateral occlusion of the iliac or femoral arteries. In advanced cases it is frequently impossible to differentiate thromboangiitis (endangiitis) obliterans (Winiwarter-Buerger's disease) clinically or histologically from the atheromatous form of arteriosclerosis (known also as arteriosclerosis obliterans). The differentiation between aortic thrombosis and obliteration of the iliac arteries is not only of theoretical interest but also of therapeutic importance. Relatively limited occlusion, for instance, in the external iliac artery is sometimes amenable to surgical treatment. Angiography permits evaluation of the function of certain parts of the vascular system. In aortic thrombosis, serial aortograms, and possibly aortography of the femoral artery, may be necessary. If pulsation is lacking in the inguinal region, an occlusion of the iliac vessels is first suspected. The author gained the impression that the development of hypertension is indicative of thrombosis of the aorta.

The author describes the history of a patient in whom the development of total obliteration of the aorta could be observed by means of aortography over a period of 2½ years. The patient had a generalized thromboangiitis obliterans that was progressive. When he was 50 years of age, there first appeared disturbances of the peripheral circulation which, despite periarterial and lumbar sympathectomy, subsequently required an amputation of the right thigh. The diagnosis could be verified by histological studies. The blood pressure was still normal at this time. Four years after the onset of the circulatory disturbance, the patient experienced symptoms of intermittent claudication on the left side, which was treated by lumbar sympathectomy on that side. After an additional 4 years, aortography revealed a narrowing of the aorta and pads in the intima of the iliac vessels on the right side as well as closure of the iliac vessels on the left side, including the femoral artery. At this time blood pressure was still normal. After another 3 years a new aortogram revealed a total aortic thrombosis immediately below the branching-off of the renal arteries. The ostiums of both renal arteries showed stenosis. Now hypertension existed —195/105 mm. Hg. In view of the generalized character of the lesion, only conservative therapy was considered. The prognosis was unfavorable. Three factors were important in this case: (1) the development of the aortic thrombosis; (2) the maintenance of the circulation by way of anastomoses in those regions of the body which because of the height of the aortic closure could not receive blood; and (3) the development of endangiitic hypertension.

Complete obliteration may begin in the aorta itself; closure of the common iliac arteries is then the result. According to a thorough review of the literature undertaken by Schrader, this is less frequent than is the primary thrombosis of one or both common iliac arteries, which by ascending advance occludes the aorta. If the stenotic process begins in one of the common iliac arteries, it may extend to the other after it has reached the bifurcation, and this makes the aortic occlusion complete. Mechanical circulatory factors presumably play a part in the frequent occlusion of the common iliac arteries. Iliac stenosis often occurs where the impact of the aortic blood strikes the vascular walls, and it has been suggested that closure of the common iliac artery is a preliminary stage of total aortic thrombosis. Obstruction of the ostiums of the renal arteries means death. Surgical treatment aims at restoration of the circulation by thromboendarterectomy, transplantation, or bypass operations, but in the patient reported only symptomatic therapy was possible, because the endangiitis obliterans was so far advanced.

Myasthenia Gravis: Results of Thymectomy. M. J. Brea, A. A. Santas and M. E. Bellizzi. Tórax 6:345-353 (Dec.) 1957 (In Spanish) [Montevideo, Uruguay].

The main causal factor of myasthenia gravis seems to be the presence of remains of the thymus, or a thymoma. The thymoma may simulate a mediastinal tumor on roentgenologic examination of the mediastinal region. In cases of myasthenia gravis, the presence of a mediastinal tumor constitutes an indication for a thymectomy. The diagnosis of a thymoma as cause of myasthenia gravis is made from the results of clinical examination, as well as from those of the prostigmine test. It is confirmed by the results of simple roentgenologic examination of the mediastinal region. Pneumomediastinum, as a diagnostic procedure, is unnecessary and is dangerous for the patient. Thymectomy is indicated in cases of myasthenia gravis (1) when the medical treatment is insufficient, as shown by the high requirements for the administration of Prostigmin; (2) when a mediastinal tumor is detected; and (3) when during the rapid course of the disease in relatively old adults a mediastinal tumor has not been found but is strongly suspected. Thymectomy should be performed when the patient is in the period of stabilization of the disease, in the absence of myasthenic crises and of respiratory complications. The operation is contraindicated in progressive forms of the disease, which do not respond to medical treatment. The technique consists of a total thymectomy by means of a middle sternotomy. Forty-three patients with myasthenia gravis, who were observed by the authors over a period of 11 years at the Clínica Médica y Quirúrgica of the Faculty of Medicine of Montevideo, had a thymectomy. No postoperative deaths occurred in any of the 30 patients in whom the disease was stabilized. Eight of the 13 patients with progressive myasthenia gravis died in a period which ranged from 24 hours to 12 days after the operation. In the group of 35 patients who recovered, the results were excellent in 13 patients, good in 9, and fair in 7, and the disease became stabilized in 7 patients. The deaths of two patients occurred 1 and 3 years, respectively, after apparently good operative results. These patients died from a recurrence of the disease, with acute respiratory symptoms. The authors conclude that thymectomy is a useful operation in the treatment of myasthenia gravis if the proper indications are observed.

Present-Day Treatment of Tuberculosis of the Principal Joints of the Limbs in the Adult. S. de Sèze, J. Debeyre and C. A. Huchet. Semaine hôp. Paris 34:1090-1101 (April 18) 1958 (In French) [Paris].

Antibiotics have revolutionized the treatment of tuberculosis of the joints in the adult. Patients in whom the disease is just beginning can be completely cured, with restoration of function in the affected joint, by medical treatment alone if the condition is promptly and accurately diagnosed. Synovial biopsy, with removal of a small fragment of the synovial membrane through a short incision over the most accessible part of the articular cavity, is a completely safe and almost always accurate procedure: only once out of some 60 biopsies were the histological findings negative when the disease was proved to be tuberculous by guinea pig inoculation. Other diagnostic methods, especially roentgenography, bacterial culture, and guinea pig inoculation, should also be used for added assurance, since no one method is absolutely reliable. Whatever the methods adopted, the diagnosis should be firmly established before antibiotic treatment is started, because antibiotics quickly efface the characteristic histological findings.

Patients in whom the disease is more fully developed still require surgical treatment, but the necessary procedures can be carried out more safely and effectively now that antibiotics are available. Preliminary antibiotic treatment quickly improves the patient's general condition, checks osseous destruction, and dries up abscesses and fistulas. The authors' patients were operated on after only one month of treatment. Mortality, which lay between 25 and 30% in most statistics before World War II, has been practically eliminated: none of the patients in this series died. The absence of postoperative fistulas and of generalization of the disease brought about by the use of antibiotics has made it possible to carry out intrafocal operations designed to eliminate the tuberculous focus and so to produce a definitive cure. Finally, the use of antibiotics has improved the functional results by permitting earlier mobilization in mobilizing operations and by making it possible to perform intra-articular arthrodeses leading to firmer and more durable ankylosis.

Symptoms After Cholecystectomy. W. Burnett and R. Shields. Lancet 1:923-925 (May 3) 1958 [London].

Symptoms continue or develop in from 15 to 20% of patients after cholecystectomy for gallstones. Postcholecystectomy symptoms are probably even commoner after cholecystectomy for noncalculous disease. These unsatisfactory results have led to use of the term "postcholecystectomy syndrome," which the authors regard as unsuitable, because in many cases symptoms precede cholecystectomy, and the symptoms are not constant enough to be regarded as a syndrome. The authors investigated the incidence and cause of postcholecystectomy symptoms in 141 of 200 patients who underwent cholecystectomy in a Glasgow hospital between January, 1950, and December, 1956. The 141 patients included 114 women and 27 men. The ages ranged from 20 to 79 years, but 79% were between 40 and 69 years. At operation, the gallbladder was diseased in 106 (75%) cases and contained gallstones in 129 (92%). It was not removed unless gallstones were present or the wall was obviously diseased. In most cases both conditions were met. The common bile duct was explored in 38 cases (27%); stones were found in 22. Twenty of 141 patients (14%) had significant symptoms after cholecystectomy. In 18 of the 20 patients with symptoms, the cause was an extrabiliary lesion, most commonly peptic ulcer. In only 2 patients could symptoms be ascribed to the biliary tract. In 4 other patients symptoms due to biliary tract disease had been relieved by a second operation before the follow-up inquiry. The authors conclude that the term "postcholecystectomy syndrome" does not seem justified.

Bilateral Pheochromocytoma in a 12-year-old Boy. C. A. Linke, I. Rosenthal and J. H. Kiefer. J. Urol. 79:781-784 (May) 1958 [Baltimore].

A 12-year-old boy became ill with headaches and blurring of vision. Urinary frequency and polyuria developed. He lost 10 lb. from February until May. On May 16 his headaches became quite severe and were accompanied by vomiting and abdominal pain. A physician noted that he had severe hypertension and arranged for hospitalization. On admission an intravenous Regitine test for pheochromocytoma was performed with the injection of 3 mg. intravenously. The test was positive. The blood pressure dropped from 180/150 to 100/60 mm. Hg in 1 minute. Retinal findings were consistent with severe hypertension, with papilledema of both disks. Regitine was given orally in gradually increasing doses until the boy was receiving 75 mg. every 2 hours. Roentgenography after a presacral introduction of air revealed a heart-shaped mass superior to the upper pole of the right kidney. The right adrenal including the tumor was resected without difficulty. The blood pressure fell after removal of the tumor to 140/100 mm. Hg, but no arterenol was administered. The peritoneal cavity was opened, but no other tumor was found by palpation, including the area about the bifurcation of the aorta and the area of the left adrenal. The patient tolerated the procedure well. The tumor was found to be a pheochromocytoma. It contained 2 mg. per gram of arterenol, and it weighed 30 Gm. Postoperative increase in blood pressure led to a new operation, during which cardiac standstill occurred. Further surgery was postponed after the heart had regained its normal rhythm.

At a later operation on this patient it was found that, just anterior and somewhat medial and quite adherent to the left kidney, there was a nodular mass, which dissection disclosed to be attached to the left adrenal in such a way that only a small area of the upper portion of the left adrenal was normal. The lower and medial portions of the left adrenal were involved in a nodular tumor, which was resected along with the entire left adrenal. An area along the aorta, just above the left renal vessels but not adherent to the left adrenal, was subjected to biopsy, because this area was somewhat thicker than expected. The biopsy disclosed the tissue to be another pheochromocytoma, which was likewise excised. The blood pressure dropped rapidly to 80/72 mm. Hg. Levarterenol (Levophed) was given intravenously. The boy recovered and was discharged. His maintenance therapy has consisted of daily oral administration of cortisone and of monthly injections of desoxycorticosterone trimethyl acetate, and he was given additional table salt with his meals.

This case illustrates that pheochromocytoma, along with renal disease, coarctation of the aorta, and essential hypertension, must be considered in the differential diagnosis of hypertension in children. As in adults, the Regitine test is valuable in diagnosis. If possible, confirmation should be obtained by the determination of catechol amine excretion in the urine, since false-positive and false-negative Regitine tests occur. Presacral air studies may locate the tumor. In pheochromocytoma in children it is of importance to note that these tumors are more likely to be in extra-adrenal sites than they are in adults; they are also more likely to be in both adrenals in children and are just as rarely malignant. Despite the difficulties involved, the pheochromocytoma of childhood is amenable to surgical cure.

An Evaluation of the Shunt Operation for Portal Hypertension. Lan Hsi-Ch'un, Tung Fang-Chung, Yao Ch'uan-Wen and others. Chinese M. J. 76:315-327 (April) 1958 (In English) [Peking].

Portal hypertension is a relatively common disease in China. In territories south of the Yangtze River its main cause is schistosomiasis, in the late stage of which the liver becomes cirrhotic and portal hypertension develops as the blood flow in the portal system is obstructed. Schistosoma ova were identified in 50% of the 124 patients with portal hypertension subjected to shunt operation. The authors believe that, if a thorough and painstaking search for schistosoma ova had been made in every patient, this incidence would have been much higher. The ages of the patients ranged from 7 to 61 years; 100 were males, and 24 were females. A history of bleeding was obtained in 78 (or 63%) of the patients. Varicosities of the esophagus and fundus of the stomach were present in 76%, and the spleen was enlarged in all cases. Only 10 of the 124 patients had ascites, as those with this condition were not generally considered suitable for a shunt operation.

Ninety-five operations were of the splenorenal type, and 27 were of the portacaval type; 1 operation was a shunt between the left renal vein and a tributary of the left gastroepiploic vein, and another operation was a shunt between the splenic vein and a large tributary of the left renal vein. The average drop of portal pressure was 16 cm. of water for splenorenal shunts and 13.5 cm. for portacaval shunts. In both types the portal pressure remained higher than the normal value immediately after operation. The portal pressure, however, will continue to drop to normal range with the lapse of time. Coma was a postoperative complication in 11 of the 27 patients with portacaval shunt, but occurred in none of the 95 patients with splenorenal shunt. Furthermore, splenorenal shunt corrects hypersplenism by removal of the spleen. Splenorenal shunt lowers portal pressure more than the portacaval does. Splenorenal shunt is the treatment of choice for portal hypertension. Portacaval shunt should be contemplated only in patients in whom the spleen has been removed or the spleen is small with a negligible degree of hypersplenism. Special attention should be paid to the diet, and administration of ammonium salts should be avoided after portacaval shunt operation.

Twelve of the 124 patients died (9.7%). The mortality from shunt operations can be reduced by refraining from them in the presence of persistent ascites or jaundice. Furthermore, the liver function tests should indicate fairly normal conditions (cephalin-cholesterol flocculation test, 3 + or less). Tissue trauma should be avoided. The routine use of the gastric tube should be discarded in order to avoid injury to the esophageal varices. Prophylactic measures should be taken against hepatic coma for patients undergoing portacaval shunt. In the follow-up of 98 patients for from 5 months to 3 years and 10 months, it was found that bleeding from the upper gastrointestinal tract developed in 5 (5.1%). One patient died of massive hemorrhage. Barium meal esophagraphy revealed marked improvement or even complete obliteration of varicosities. Shunt by reducing the portal pressure can arrest bleeding quite effectively, but it will not alter the pathological changes in the damaged liver. Shunt operation, because of its complicated procedure and prolonged ether anesthesia, is liable to aggravate liver damage. This deserves further study.

End Results of Pulmonary Resection for Tuberculosis. J. A. Moore, H. E. Walkup, J. E. Rayl and J. P. Chapman Jr. Ann. Surg. 47:659-667 (May) 1958 [Philadelphia].

During the 10-year period from Jan. 1, 1947, to Jan. 1, 1957, 1,130 pulmonary resections were carried out on 1,080 patients at the Veterans Administration Hospital at Oteen, N. C., and at the Western North Carolina Sanatorium at Black Mountain, N. C. The treatment of tuberculosis and the surgical techniques differed very little in these 2 institutions, and so the patients are analyzed as 1 group. Records of 894 of the 961 surviving patients (93%) were available for follow-up study. During the early part of the period under consideration, pulmonary resection was resorted to after all other therapeutic measures, including thoracoplasty, had failed. Later, resections were done in preference to theoracoplasty. Streptomycin, used as a prophylactic agent, was given prior to surgery, and its administration was continued for 2 to 4 weeks after operation. From 1951 to 1953 small nodular lesions were removed by segmental or wedge resection. It was soon evident that surgical complications were as great as the recurrence rate of these tubercular lesions. As additional drugs came into use, more patients were treated by these agents for longer periods of time, so that during the past 2 years the authors have operated only on patients who are classed as failures of antimicrobial therapy. [Today this failure is the most frequent indication for excisional surgery.] The antituberculous drugs have been used according to various protocols to determine the proper dosages and length of treatment, and gradually they have been used for longer and longer periods of time and in various combinations.

The incidence of complications, the mortality, and the long-term follow-up results are correlated with the type of resection and the duration of preoperative drug therapy. The increased incidence of complications and morbidity in the retreatment of patients with drug-resistant organisms undergoing excisional surgery is emphasized. The hazard of development of a bronchopleural fistula and/or empyema after a lobectomy plus a segmental resection (28%) is greater than that encountered after a pneumonectomy (24%). The follow-up study revealed that 22% of the surviving patients who had a lobectomy plus a segmental resection still had active tuberculous disease of the lungs. A plea is made for surgical-medical consultation between the 4th and the 6th month after onset of antituberculous drug therapy. This early evaluation would enable the surgeon to select treatment-failure patients for surgery before tubercle bacilli become resistant to the antituberculous agents.

Experiences with General Prophylaxis Against Thrombosis, with a Report on 3,000 Patients Treated with a Hydroxycoumarin Derivative (Marcumar). W. Cramer and E. Pohlhaus. Beitr. klin. Chir. 196:1-18 (No. 1) 1958 (In German) [Munich, Germany].

The definite increase in the incidence of thrombosis and pulmonary embolism which was observed among patients in the West End Hospital in Berlin in the period after World War II, and which corresponded with observations made in other cities and countries, prompted the authors to start general prophylactic treatment against thrombosis at the surgical clinic of the Free University in Berlin in 1954. This treatment included early rising on the first postoperative day and, on the second or the third day after major operations, exercises in bed and administration of anticoagulants. Of 3,455 patients who were thus treated, 3,194 received, predominantly or exclusively, a hydroxycoumarin derivative, Marcumar [3-(1-phenylpropyl)-4-hydroxycoumarin], as an anticoagulant.

All patients who were over 30 years of age and who were expected to be confined to bed for a prolonged period were treated by this method. Excluded were patients with severe hepatic damage, renal damage, hemorrhagic diathesis, severe arteriosclerosis, incurable carcinoma, and those who had undergone cardiac or vascular surgery. Only 3 of the patients treated with anticoagulants died of pulmonary embolism, while 16 of those from whom anticoagulant therapy was withheld because of contraindications died of pulmonary embolism; pulmonary infarcts occurred in 24 additional patients and severe thrombosis in 8 who had not received anticoagulant therapy. The incidence of thrombosis and pulmonary embolism, and particularly that of fatal pulmonary embolism, thus was definitely reduced by anticoagulant therapy. Prophylactic treatment with anticoagulants was complicated by the occurrence of hemorrhages in 72 patients (2.2%); the hemorrhages were severe in 17 patients (0.53%), and 3 of these died. Emphasis is put on the fact that not every hemorrhage is due to the administration of anticoagulants, but great care must be taken to determine the Quick values immediately when inspection of the operative wound reveals recent subcutaneous blue discoloration. On the whole, the general prophylaxis has proved valuable.

NEUROLOGY & PSYCHIATRY

The Effect of Focal Intracranial Lesions on High Blood Pressure. A. M. Ostfeld. Am. J. M. Sc. 235: 539-548 (May) 1958 [Philadelphia].

Blood pressure changes after various types of frontal lobe surgery have been correlated with concurrent personality alterations. It has generally been observed that a transient fall in blood presssure occurred after such surgery, together with a decrease in anxiety. A fall in blood pressure, together with specific changes in attitude and behavior, has also been reported after psychotherapy. A group of untreated hypertensives, in whom specific personality and behavior changes followed intracranial lesions of known size and location, and in whom diet (including salt intake), body weight, and renal status were essentially unchanged, were studied. For this purpose the hospital records of all patients undergoing craniotomy at the University of Illinois Neuropsychiatric Institute during the past 10 years, 806 in number, were examined. The 14 subjects selected had hypertension of known duration and severity which antedated neurological symptoms. Clinical and laboratory evaluation confirmed the absence of prior renal disease, toxemia of pregnancy, or other specific causes for the elevated blood pressure. Four patients were without significant cranial damage prior to surgery; on 2 of them bilateral frontal lobe surgery was performed for pain syndromes, and on the other 2 a temporal lobectomy for psychomotor seizures was done. There were 5 patients with meningioma, 2 with acoustic neuroma, and 1 with hemorrhagic cyst at the site of an old cerebral vascular accident; in 2 patients there was focal softening after intracranial vascular accident. The site and extent of each lesion were assessed.

In 12 of the 14 patients with essential hypertension, blood pressure and state of hypertensive disease were largely unchanged 1½ to 7 years after varying degrees of intellectual and social deterioration occurring in association with focal brain damage. The 2 subjects whose blood pressure fell notably exhibited a very large lesion, drastic mental deterioration and personality change, and a stable and secure social environment. The capacity to respond to a psychologically stressful interview with acute pressure elevations persisted after unilateral frontal lobe loss, but in one patient with bilateral frontal lobotomy and in another with extensive parietal lobe damage and personality deterioration no such pressor response occurred. Blood pressure was apparently in part maintained by neurogenic mechanisms in 2 subjects with moderately extensive unilateral or bilateral frontal lobe damage. The foregoing data support the thesis that no one part of the cerebral cortex is preeminently important in mitigating or maintaining hypertension or the capacity to respond to stressful events with pressor episodes.

Late Sequelae After Cerebral Fat Embolism and Aeroembolism. W. Neugebauer. Beitr. klin. Chir. 196:43-60 (No. 1) 1958 (In German) [Munich, Germany].

The author reports on 5 men, between the ages of 19 and 49 years, with late sequelae after cerebral fat embolism and on 3 patients, a 31-year-old woman, a 21-year-old man, and a 7-year-old girl, with late sequelae after aeroembolism. The first of the 5 men sustained an injury of his left upper extremity by a fragment of shell in the war, but he did not sustain a cranial injury. One hour later progressive clouding of consciousness occurred, which was followed by unconsciousness for 9 days. Several months later epileptic equivalents were observed, and gradually severe epileptic attacks occurred with increased frequency until an organic psychotic syndrome caused complete incapacity of being gainfully employed. In the absence of any evidence of vascular atrophy of the brain and of neoplastic growth, the prolonged unconsciousness suggested that fat embolism had resulted in multiple diffuse focal lesions and edema of the brain, with an atrophic cerebral condition, the typical organic psychotic syndrome, and seizures as sequelae. The second of the 5 men had an automobile accident with multiple rib fractures, fractures of the pelvis, and central dislocation of the left hip joint; a shock syndrome occurred which was followed several hours later by unconsciousness for 5 days, associated with severe psychomotor unrest. Two years later increasing weakness of cerebral function and epileptic equivalents were observed. Of the remaining 3 men, 2 had been buried alive by a collapsing building and by a collapsing bunker, respectively, and the third had been hurled a distance by a factory explosion; all 3 had sustained various contusions of the body but no cranial injury. In these 3 men typical organic psychotic syndromes occurred, similar to those observed in the 2 previously reported patients. All 5 men received surgical treatment corresponding with their injuries, but neurological examination and treatment were omitted.

The fact that unconsciousness occurred only gradually and several hours after the accident shows that it requires some time until fat enters the brain. Occlusion of vessels by emboli, circulatory disturbances of the brain, and cerebral edema are responsible for the sequence of events, i. e., unconsciousness followed by a loosening phase with delirium, and return of consciousness. The multiple, and perhaps even miliary, emboli were responsible for the epileptic seizures which occurred in 4 of the 5 patients and for the repeated attacks of excitation in the 5th patient. Symptoms of multiple small focal lesions caused temporary suspicion of multiple sclerosis in 1 patient. The organic psychotic syndrome in all 5 patients consisted of dedifferentiation, levelling, reduced performance, disturbances of memory, and disturbances of affectivity. The elucidation of these late sequelae after cerebral fat embolism is extremely difficult, particularly if neurological and mental manifestations, which often may be atypical, occur gradually after contusions of the body in the absence of any cranial injury.

Elucidation of the late sequelae in the 3 patients with aeroembolism was somewhat less difficult. In the woman, sudden unconsciousness was associated with a severe uterine hemorrhage several days after an abortion. The evacuation of the uterine cavity was associated with entering of air and cerebral aeroembolism resulting in permanent damage, which was revealed as brain atrophy by pneumoencephalography. Seizures and an organic psychotic syndrome remained as late results. In the man, a gunshot injury, with the projectile remaining in the right lung, was followed by unconsciousness for several days. On return of consciousness a central unilateral paralysis was observed, which continued unchanged for many years. The pulmonary injury had caused aeroembolism of the greater circulation. The girl was hurled around by the blast of an aerial mine; she fell on the right temple, but remained conscious and did not bleed from the nose, ears, and mouth. Sudden unconsciousness occurred the next day and was followed by petit mal attacks. Four years later severe generalized seizures occurred. The explosion had resulted in interstitial pulmonary emphysema caused by acute abnormal inflation of the lung; air then entered the pulmonary veins and caused cerebral aeroembolism. Psychomotor epilepsy resulted from central damage which apparently occurred in the thalamic nuclei. Trephining and exposure of the right temporal lobe did not show any contusion foci in the temporal and basal-frontal regions of the brain. Widening of the ventricles was caused by atrophy. The knowledge of these disease aspects is of great importance for their diagnostic evaluation.

Echo 9 Virus Infections in Eastern Canada: Clinical and Laboratory Studies. A. J. MacLeod, R. S. Faulkner and C. E. van Rooyen. Canad. M. A. J. 78:661-665 (May 1) 1958 [Toronto].

Enteric cytopathogenic human orphan (ECHO) virus, type 9, was isolated from 27 male and 13 female patients with aseptic meningitis who were studied clinically. Thirty-three of the 40 patients were less than 15 years of age. Headache, nausea and vomiting, stiffness of the neck, and muscle pains were prominent symptoms. Moderate fever, nuchal rigidity, and normal reflexes were cardinal physical findings. A maculopapular rash was noted in 10 patients. A pleocytosis of the cerebrospinal fluid featuring mononuclear cells was a constant finding. Virus was readily isolated from the cerebrospinal fluid, stools, and throat washings on monkey kidney and human amnion cells in primary culture. The serologically typed ECHO 9 viruses were shown to be pathogenic to infant mice. Many of these cases could have passed unnoticed as examples of severe headache, except for the fact that the attention of local clinicians had been focused on the disease and a search for patients was conducted. The high incidence of isolation of virus from the cerebrospinal fluid emphasized the value of virologic examination of the latter in all patients with severe headache of idiopathic character. The rash observed in these patients bore a close similarity to that of rubella, and it is not improbable that the 2 diseases have been confused in the past. Whether or not the 2 diseases may have an identical causative agent remains open to conjecture. Roseola infantum merits similar consideration.

PEDIATRICS

Abdominal Pain of Cerebral Origin in Children. J. S. Prichard. Canad. M. A. J. 78:665-667 (May 1) 1958 [Toronto].

The author reports on 19 children with abdominal pain of cerebral origin. These patients were divided into 2 groups. The first group consisted of 17 children in whom the attacks of abdominal pain lasted 1 hour or longer and were frequently accompanied by pallor, headache, nausea, or vomiting. The child was usually drowsy and fell asleep; upon awakening, he was generally normal. Most of the patients had a family history of migraine. The electroencephalogram was normal or showed a mild, generalized dysrhythmia. In the second group, consisting of 2 children, the attacks were characteristically much shorter, lasting from 5 to 10 minutes only. They consisted of a sudden onset of abdominal pain, some confusion, and pallor. The attack was often followed by drowsiness. The electroencephalogram showed a focal abnormality in the temporal region. A family history of migraine was uncommon.

It is suggested that the children in the first group had "abdominal migraine" and those in the second group had true "abdominal epilepsy." In many respects the attacks are similar in both groups. The cerebral site is probably identical and lies in the region of the insula. It is the mechanism of production of the abnormal cerebral function that is different in the 2 groups. The treatment of abdominal epilepsy is the same as the treatment of any other type of epilepsy. It consists essentially of administration of anticonvulsants and, in rare cases, cortical excision. In the treatment of abdominal migraine, drug therapy plays but a small part. In patients with longer attacks, the administration of a preparation of caffeine and ergotamine (Cafergot) can occasionally inhibit the attack, if the drug is given at the onset. In some patients, continuous administration of small doses of phenobarbital or diphenylhydantoin (Dilantin) sodium is of value. In most patients the attack may continue despite medication. From a therapeutic point of view it is a mistake to call the disease in patients belonging to the first group "epilepsy," because the anxiety so engendered in the family group tends to make attacks more frequent. A fundamental of treatment is to have the parents understand that the child should lead a normal life and that the attacks, while tiresome, are benign. To establish the correct causative factor is of greatest importance for the management of the patient.

Use of Antibiotics in Treatment and Prophylaxis of Bacterial Endocarditis. R. Laplane, P. Debray and R. Salbreux. Nourrisson 46:59-65 (March-April) 1958 (In French) [Paris].

The authors report on 67 children with bacterial endocarditis who were treated with phenylbutazone as anti-inflammatory agent and benzathine-penicillin G as prophylactic agent against group A streptococcic infection for periods varying from 1 to 3 years. Anti-inflammatory treatment was instituted at the same time as the antibiotic treatment. Of the 67 children, 40 (59%) were treated for more than 2 years. In all the patients determinations of the antistreptolysin titer were carried out regularly regarding immunity, and the course of the inflammation was followed by regular determinations of erythrocyte sedimentation rate, fibremia, haptoglobin index, and paper electrophoresis. Phenylbutazone was administered for about 4 weeks. At the same time 1 million units of penicillin G was given intramuscularly daily for 10 days, being followed by 2.4 million units of benzathine penicillin G given intramuscularly every 3 weeks as prophylactic treatment. For 8 days preceding each of the benzathine penicillin G injections, 300,000 units of penicillin V was given daily in 3 divided doses by the oral route. There was no recurrence of rheumatic fever or failure of treatment in any of the 67 children. No new cardiac lesions occurred, and there were no allergic reactions to the treatment. Normalization of the antistreptolysin titers could be observed. The children were discharged after 5 to 8 weeks of hospitalization when the biological inflammation had returned to normal, and they were able to attend school after a period of about a month of convalescence. Despite the highly satisfactory results complete absence of streptococci in the pharynx may not be assured. In 3 children beta-hemolytic streptococci were detected, but not being of group A they were not considered rheumatogenic. In 7 children a temporary and isolated rise of antistreptolysins occurred in the course of the prophylactic treatment. Penicillin V produced nausea in some children, but they were easily cured with symptomatic treatment. It seems that the danger of recurrences of rheumatic fever decreases after 5 years, and the prophylactic treatment then can be discontinued. The success of this treatment depends largely on the patient's strict adherence to this regimen without interruption and on the early institution of the treatment with adequate doses of antibiotics. Combined anti-inflammatory and prolonged antibiotic treatment is indispensable.

DERMATOLOGY

Cutaneous Porphyria with Porphobilinogenuria: A Review and Report of a Case Treated by Chelation. S. M. Woods, H. A. Peters and S. A. M. Johnson. A. M. A. Arch. Dermat. 77:559-567 (May) 1958 [Chicago].

The patient presented, a 16-year-old youth, had hepatic porphyria of the cutanea tarda variety, with evidence of latent and manifest porphyria in the maternal blood line. The patient was studied clinically, biochemically, and histologically over a period of 2 years, during which time the authors observed the emergence of porphobilinogenuria and manifestations suggesting that the syndrome may be merging into that which is seen in mixed porphyria, where abdominal or neurological manifestations may coexist or alternate with cutaneous symptomatology. It is believed that this represents the first report of quantitative studies of urinary porphobilinogen and its precursor, δ-aminolevulinic acid, in a patient with cutaneous porphyria under prolonged study.

Chelation therapy with heavy-metal chelates, such as dimercaprol (BAL) and edathamil calcium-disodium (Calcium Disodium Versenate), had been used by the authors in the treatment of acute intermittent hepatic porphyria and had proved highly favorable and often dramatic in 14 of 21 patients so treated. A number of these patients were moribund, while under steroid and other forms of therapy, until chelation was begun. Because of this experience, a program of chelation therapy and study was undertaken in the patient herein reported. This patient provided an unusual opportunity to observe the transition of cutaneous porphyria into a mixed porphyria with porphobilinogenuria. His apparent favorable response to edathamil calcium-disodium was encouraging and has suggested the need for further evaluation of chelation therapy in the treatment of porphyria.

Dynamics of Autosensitization Dermatitis: A Clinical and Microscopic Concept of Autoeczematization. A. W. Young Jr. A. M. A. Arch. Dermat. 77:495-502 (May) 1958 [Chicago].

Autoeczematization is the process by which a widespread dermatitis may complicate several types of localized eczema. Generalized autogenous eczema describes the disseminated disorder. This report deals with the clinical history, course, and development of the syndrome and with the microscopic picture of various types of lesions to be found in the diffuse and often generalized eruption. Relationships among generalized autogenous eczema, disseminated and circumscribed neurodermatitis, nummular eczema, and exudative discoid and lichenoid chronic dermatosis are discussed. Studies were made on 60 persons (33 women and 27 men) in whom generalized autogenous eczema developed. Thirty-six patients either recalled eczema as a child or had hay fever or a history of allergy in the family. In 7, the history of an allergic background was highly suggestive; in the remainder, no such history could be elicited. In general, the initial localized eruption was a recurrent or persistent condition of long standing and suggested various diagnoses, such as nummular eczema, stasis or neurostatic dermatitis, lichen chronicus simplex, contact dermatitis, dry eczema of hands or legs, axillary dermatitis, scrotal eczema, and so on. In most patients, the dermatitis was acute, weeping, vesicular, and crusted prior to the onset of autoeczematization, which followed the exacerbation by a few days to a week or more.

Generalized autogenous eczema is a dynamic syndrome which is best appreciated by viewing the disorder as it progresses through its various stages, which are usually the following: vesicular, organizing, confluent (spreading), multiform (diffuse), and resolving (generalized). Early recognition of the syndrome in the vesicular stage or stage of organization, accompanied by adequate treatment, may halt further extension of the process. On the other hand, when the multiform (diffuse) stage is reached, in which there is an intermixture of desiccating lesions and eczematoid patches kept alive by scratching and rubbing, ill-advised medication, and secondary infection, a second cycle may be initiated, with the formation of new vesicles. Clinically, there is a close relationship among stages of generalized autogenous eczema, neurodermatitis, nummular eczema, exudative discoid and lichenoid chronic dermatosis, and dermatitis herpetiformis. These dermatoses commonly have an allergic background and are often associated with emotional problems. A basic microscopic process may be found throughout, although individual variations can be seen. These observations suggest that neurodermatitis, nummular eczema, exudative discoid and lichenoid chronic dermatosis, dermatitis herpetiformis, and generalized autogenous eczema belong to the same group of diseases.

Erythema Multiforme Exudativum (Stevens-Johnson Syndrome): Report of Two Cases with Postmortem Findings and Comment. F. M. O'Connor. A. M. A. Arch. Dermat. 77:532-541 (May) 1958 [Chicago].

Since 1922, when Stevens and Johnson reported on 2 extremely ill children as having "eruptive fever" with stomatitis and ophthalmia, sporadic reports have appeared on this serious and at times fatal disease. Recent reports in the literature seem to indicate that steroid therapy is of value in this condition. This report presents 2 cases of erythema multiforme exudativum (Stevens-Johnson syndrome), with postmortem findings, in which steroids, antibiotics, and supportive therapy failed to halt the progress of the disease. The 2 patients were women, aged 27 and 31 years respectively. The rapidity of the downhill course in both was amazing in view of the lack of bacteriological, biochemical, and x-ray findings sufficient to justify such a rapid termination. The exact cause of death was unknown. Postmortem findings threw no light on the causation. Erythema multiforme exudativum was first described by Hebra in 1860 as an illness characterized by pleomorphic lesions confined to the skin. Later other terms were introduced to describe the same general pattern or slight variations. Thus, Fiessenger and associates in 1923 added the term "ectodermosis erosiva pluriorificialis"; Stevens and Johnson in 1922 reported "a new eruptive fever"; Baader in 1925 coined the expression "dermatostomatitis"; Behcet in 1937 suggested the "triple symptom complex"; Stanyon in 1945 used the term "mucosal respiratory syndrome"; and in 1950 Robinson and associates suggested the term "mucocutaneous ocular syndrome." Basically, all these conditions are variations of erythema multiforme. Physicians should be able to recognize the variants. For purposes of clarification and because all the entities are of the same basic pattern, varying only in the degree and severity of their reaction, an all-inclusive term, "ocular mucocutaneous syndrome," might be preferable.

UROLOGY

Endometriosis Vesicae: 77th World-Wide Observation. J. Picatoste Patiño. Acta urol. belg. 25:318-325 (July) 1957 (In French) [Brussels].

The author presents observations on a 39-year-old nulliparous woman with endometriosis vesicae, which constitutes the 77th report of this disease in medical literature. The patient, who had been subjected to ovariectomy on the left side a few years before because of inflammation of the adnexa and ovarian endometriosis with "chocolate cysts," complained that every month for the last 5 years, 4 to 5 days before menstruation, she began to have pains and a burning sensation at urination, with frequent and increased miction and a feeling of heaviness in the perineum. These disturbances were intensified during the menstrual flow but diminished during the following days. About a week after the periods, her condition was normal again. Cystoscopic examination revealed 7 or 8 cysts of various sizes with normal mucous membrane. Around the cystic zone, however, excessive congestion of the vesical mucosa was evident, a fact never before observed in patients with endometriosis vesicae. Histological study of a biopsy specimen revealed glandular formations, with an epithelial covering of the endometrial type, among the bundles of smooth muscle fibers. Some of these glands were greatly enlarged and more or less completely filled with blood. The quantity of cytogenous tissue surrounding the glandular formations was surprisingly small. Changes in the cystoscopic picture generally correspond to the day of the menstrual cycle on which the examination is made; consequently, the diagnosis may be difficult to make during quiescent periods when the vesical mucosa may have a completely normal appearance. Most of the patients have a gynecologic history of disturbances believed to have predisposed them to the disease.

Bilateral Squamous Cell Carcinoma of the Kidneys. I. M. Thompson, J. Schneider and L. C. Kavan. J. Urol. 79:807-810 (May) 1958 [Baltimore].

The simultaneous occurrence of carcinoma in both kidneys is rare, the literature to date containing reports of only 10 cases. All of these were of the hypernephroid type, renal-cell adenocarcinomas. The authors describe what they believe to be the first reported instance of bilateral squamous-cell carcinoma of the kidneys. The patient was a 52-year-old man who was admitted to the urology service of the University of Texas Hospital with a history of recurrent, gross, painless hematuria for approximately 5 months prior to admission. Epigastric pain associated with nausea and vomiting was prominent and of recent occurrence. There had been moderate weight loss associated with gradual general physical debilitation. In view of the elevated nonprotein nitrogen value, retrograde urography was undertaken, first on the left side and on a subsequent day on the right. The pyelograms revealed compression distortions of the pelviocalyceal systems, sufficient to suggest bilateral infiltrating parenchymal lesions. The possibility of simultaneous neoplastic involvement of both kidneys was entertained, but in view of the hopelessness of such a diagnosis, other possibilities were broached, and measures taken to exclude entities amenable to therapy. Tests excluded tuberculosis, actinomycosis, histoplasmosis, coccidioidomycosis, brucellosis, and lymphomatous involvement.

To make sure that therapy was not being withheld from an obscure inflammatory lesion, bilateral renal exposure via the vertical approach of Simon was undertaken. Both kidneys were enlarged, pale, and turgid. Tissue removed for biopsy was seemingly grossly caseous. The pathologist's report identified the material from each kidney as undifferentiated carcinoma. Progressive general physical deterioration continued, and the patient died 29 days after admission to the hospital. Postmortem examination revealed widespread carcinomatous involvement of the liver, adrenals, and periaortic structures, as well as extensive infiltration of both kidneys. Four divergent areas of pulmonary metastasis were noted. The sequence of events was postulated as a migration of renal pelvic squamous-cell carcinoma on the right across the midline and into the hilar region of the left kidney.

INDUSTRIAL MEDICINE

An Often Unrecognized Manifestation of Pneumoconiosis in Miners: Aseptic Liquefaction of Pseudotumoral Formations. C. Gernez-Rieux, E. Balgairies, P. Fournier and C. Voisin. Semaine hôp. Paris 34:1081-1089 (April 18) 1958 (In French) [Paris].

The tumoral forms of pneumoconiosis in coal miners deserve particular attention because of the diagnostic, prognostic, and pathogenic problems they present. Do the pseudotumoral images sometimes evident in roentgenograms always correspond to the clearly delimited, dense, round or oval masses contrasting strongly with the parenchyma of the lung found in tumoral pneumoconiosis? What is their frequency and in what manner do they appear? How are they related to the intrapulmonary accumulations of fluid described by anatomopathologists and often seen by the authors in their patients? Routine examination and prolonged observation of 5,131 coal miners in northern France known to have pneumoconiosis, data obtained by transparietal punch biopsies and by surgical biopsy, when necessary, in cases presenting diagnostic difficulties, and the study of excised lung specimens have provided the authors with answers to some of these questions.

The so-called coal nodule of Gough is the basic lesion of coal miners' pneumoconiosis, which differs unmistakably from the silicosis of workers in stone. Coal miners' pneumoconiosis may take the form of progressive massive fibrosis, with or without the formation of tumoral masses. Massive fibrosis was found in 690 of the 5,131 miners studied, and 374 (52.2%) of these presented pictures of the tumoral type. The tumoral lesions appear after an average period of about 25 years, generally as the result of coalescence between large nodules. The clinical picture is not characteristic: for many years, the patient may complain only of dyspnea on effort and of expectoration of mucus occasionally tinged with blackish particles. Pleurodynia sometimes occurs. Mycobacterium tuberculosis could not be demonstrated in these patients, even by repeated bacteriological studies, including culture and guinea pig inoculation. Histological examination of biopsy specimens revealed typical fibrotic-coniotic accumulations, with anthracosis predominating in some and fibrosis predominating in others. The recovery of fluid by transthoracic puncture in 16 patients proved that in some cases the characteristic tumoral images in roentgenograms correspond to encysted intrapulmonary collections of fluid. Spontaneous evacuation, in whole or in part, of the fluid contained in these pseudotumoral lesions produces pictures typical of pulmonary excavation, but when the fluid remains latent, transthoracic puncture is the only method by which its presence can be detected. Evacuation, which takes the form of melanoptysis, may be preceded by a period of weight loss and exacerbation of dyspnea, cough, and pleurodynia. The quantity of black fluid evacuated varies; in one of the authors' patients it amounted to 500 cc. a day. The melanoptysis usually continues for several days, after which expectoration diminishes and resumes its usual characteristics; cough disappears; the temperature returns to normal; and improvement takes place in the clinical signs. The long-term prognosis depends chiefly on the slow but inexorable progress of the massive fibrosis with its severe functional complications, both respiratory and cardiovascular.

The similarity that exists between the chemical composition of the intrapulmonary fluid and that of blood plasma suggests that the intrapulmonary collections are due to transudation of plasma from the healthy lung toward the massive lesions, possibly as the result of an allergic process caused by autosensitization of the body to proteins denatured by the injurious effect of the coal dust. Isolated pseudotumoral lesions should be excised if the patient's condition is such that he can stand an operation. Excision is especially advisable in patients subject to recurrent melanoptysis or repeated hemoptysis, because it is the only method by which the patient can be cured and the otherwise inevitable development of generalized progressive fibrosis prevented.

The Treatment of Exposure to Thorium and Uranium with a Chelating Agent and Supportive Measures. W. N. Young and H. A. Tebrock. Indust. Med. 27:229-232 (May) 1958 [Chicago].

The authors report on 4 persons who were severely injured when they were exposed to thorium and uranium dusts in an explosion of 40 lb. of thorium dioxide and a much smaller quantity of uranium dioxide. The explosion occurred when these finely divided compounds, probably contaminated by nitrates, were being subjected to a burning process. Second-degree or third-degree burns were sustained by all the patients. These burns constituted the major problem, apart from the toxic action of the 2 metals. Uranium and thorium are primarily alpha emitters, and, in consequence, their depth of penetration was not below the unbroken skin; therefore, the material which covered the skin surface after the explosion was not considered biologically harmful and was removed by washing with soap and water. What was harmful was the uranium and thorium dust which the patients inhaled at the time of the explosion.

The use of chelating agents for the removal of heavy metals has been reported before, especially in the case of lead poisoning. One of the most promising chelating agents is ethylenediaminetetraacetic acid (EDTA), which combines with ions of the heavy metals to form complexes known as chelates. This chelating agent was administered to the 4 patients, 1 Gm. being diluted in 500 cc. of 5% dextrose solution and given intravenously twice daily. After 5 days this treatment was interrupted, to be resumed again after a rest period of 1 week. The chelating agent removed the uranium and thorium from the body without causing side-effects. All but 1 of the patients recovered.

Pulmonary Silicosis due to Aspiration of Abrasive Powder: Early Appearance and Rapidly Fatal Course. R. V. Vaccarezza, O. C. Croxatto and R. Coira. Medicina, Buenos Aires 17:193-208 (Aug.) 1957 (In Spanish) [Buenos Aires].

Pulmonary silicosis develops after several years of exposure to the causal agent. The disease follows a chronic course. There is an acute form of the disease with a period of exposure which varies between 4 and 18 months, a period of latency of 2 to 4 months, and a duration of the disease of no more than 1 year. A case of acute pulmonary silicosis is reported. The patient started working in a factory manufacturing abrasive soap at the age of 25 years. He used a mask during work but still complained about heavy inhalation of dust. After 18 months he began to complain about cough, asthenia, nausea, frequent vomiting, and rapid loss of weight. Dyspnea and irregular fever appeared a few months later. Serial roentgenograms showed advanced silicotic pulmonary lesions. The first roentgenogram, which was taken on the appearance of the first symptoms of the disease, showed only a slight increase of the pulmonary network in the lower field of the lungs. The second roentgenogram, taken 8 months later, showed diffuse miliary nodules. The third roentgenogram, taken a few months after the second, showed massive opacity of both lungs. The patient never had symptoms or signs of cardiac insufficiency. He died in anoxia. Tubercle bacilli were not found in the sputum or in the liquid obtained by bronchial lavage during the life of the patient. They were not found at histological study of the pulmonary and lymph node lesions at autopsy. The histopathological diagnosis was that of pure acute silicosis.

THERAPEUTICS

Regulation of Cholesterol: Prevention of Atherosclerotic Disorders (Preliminary Report). G. Salas Rivero, A. Karl and J. de Guzman. Rev. méd. Hosp. Gen. 21:281-293 (April) 1958 (In Spanish) [Mexico City].

Atherosclerosis is due to a disorder of the cholesterol metabolism in the presence of intimal changes of the large and medium-sized arteries. Four patients, between the ages of 49 and 77 years, with disorders of the cholesterol metabolism and atherosclerosis were observed. The patients had myocardial lesions and coronary sclerosis. One of the patients also had sclerosis of the aorta, obliterating endarteritis in the legs, and progressive lenticular degeneration (Wilson's syndrome). The patients were treated with toluylmethylcarbinol. The drug was given in daily doses of 0.250 Gm., in 2 fractional doses of 0.125 Gm. each, at intervals of 12 hours. Determinations of the cholesterol level of the blood were made on the 10th, 11th, and 15th days after starting the treatment. There was a marked lowering of cholesterol in the blood, especially of the ester fraction. The greatest diminution of cholesterol in the blood was reached on the 30th day of treatment. Continuation of the treatment for 10 more days resulted in stabilization of the cholesterol level. If the treatment was discontinued before the 30th day, the cholesterol values started increasing slowly, reaching the figures which were present before the treatment in about 1 or 2 months after its discontinuation. The beta-lipoproteins diminished between 22.3 and 30.9%. The ratio of lipoproteins to cholesterol became normal in the course of treatment in the 4 patients. Decreasing the cholesterol values of the blood and normalization of the lipoprotein-cholesterol ratio were associated with a marked improvement in the symptoms. The drug was well tolerated. This is a preliminary report.

Rational Basis and Practical Application of Prednisone as Antiedemic and as Diuretic Agent. M. Ficini and M. Ricci. Sett. med. 45:653-661 (Dec. 31) 1957 (In Italian) [Florence, Italy].

Thirty-three patients who had various diseases associated with edema were placed on prednisone therapy. Biliary cirrhosis with ascites was present in 8 patients, aged between 43 and 73 years, 7 of whom had Laennec's cirrhosis and 1 had hepatosplenomegaly. The patients received the drug in daily doses of 30 to 40 mg. for a minimum period of 10 days. Improvement in well-being and return of appetite resulted in all. However, the diuretic improvement in patients with Laennec's cirrhosis was insignificant, except that daily flow of urine increased by 20% in 1 patient. A considerable increase in excretion of water (100%) and of sodium was observed in the patient with hypertrophic cirrhosis; the improvement persisted for 2 months after withdrawal of prednisone.

Prednisone was administered to 11 patients with congestive heart decompensation in daily doses of 25 to 30 mg. for a period of 10 to 20 days. There was a prompt and marked diuretic response in all the patients of this subgroup, which effect persisted after withdrawal of the drug. Prednisone induced responsiveness to mercurial and other types of diuretics in 6 patients of this subgroup, who had previously been refractory to them. Prednisone was also given to 14 women with premenstrual disturbance during the 7 days preceding menstruation. It produced improvement in well-being and increased diuresis during the period of treatment. The sense of pressure on the chest and on the lower part of the abdomen, which was common in the past, did not recur during prednisone therapy. There was also a slight but stable loss of weight. The authors suggest use of prednisone when edema is a symptom of another pathological state and, in particular, when patients with edema are refractory to mercurial diuretics.

The Clinical Applications of Chlorotrianesine. A. Ravina and J. Ravina. Presse méd. 66:761-763 (April 30) 1958 (In French) [Paris].

Chlorotrianisene (Tace) has been used by the authors during the last 3 years in about 100 patients requiring estrogen treatment for various reasons. Tace is apparently an excellent endocrine preparation which may, in fact, be regarded as an oral implant, because it is first stored up in the body fat and then released gradually over a long period. This property of gradual release makes it particularly useful in treating hormonal disturbances in women, especially during the menopause, when treatment must often be prolonged. Tace was given to 47 women in whom the menopause was natural and to 7 in whom it was surgically induced. These patients were given 1 or 2 capsules (12 or 24 mg.) a day, by mouth, for from 30 to 60 days, according to the intensity of the menopausal disturbances and the rapidity and efficacy with which the drug acted to relieve them. Hot flashes and sweating disappeared permanently in 12 patients after treatment for 1 or 2 months. Temporary relief from these symptoms lasting for 2 or 3 months was obtained in 22 patients; for 5 or 6 weeks in 13; and for 1 month in 7. A second course of treatment, when needed, was always much shorter than the first, consisting only of 12 or 24 mg. a day for from 5 to 20 days. Tolerance for the drug was excellent in 95% of the patients. Confirmatory evidence of the estrogenic action of Tace was obtained by studies of the vaginal cytology in 30 of the patients. The results, in most cases, paralleled the clinical findings.

The effect of Tace on lactation was studied in 30 women in whom breast-feeding was contraindicated for various reasons, local or general. The best results in these patients, as in the cases reported in the literature, were obtained when the drug was given in relatively large doses and soon after delivery; in 4 patients, however, the treatment was effective even though it was not started until the second day. The best dosage seems to be at least 4 capsules a day for 7 days (daily dose, 48 mg.; total, 336 mg.). This dosage also had a simultaneous effect on the lochia, which became less profuse and sanguinolent.

Finally, 6 men with prostatic cancer and 7 women with recurrences of, or metastases from, certain cancers of the breast were also benefited, to a greater or less degree, by the administration of Tace. The results in 3 of the women, all of whom had widely ulcerated breast cancers or extensive osseous metastases, were particularly significant, with a reduction in the size of the lesion, noticeable improvement in the general condition, and regression of the functional symptoms, especially pain.

Alopecia Following Treatment with Dextran Sulphate and Other Anticoagulant Drugs. G. R. Tudhope, H. Cohen and R. W. Meikle. Brit. M. J. 1:1034-1037 (May 3) 1958 [London].

Of 87 patients who were treated with anticoagulant drugs at the United Sheffield Hospitals in England, 15 received intravenously a total dose of 90,000 units or more of dextran sulfate, 12 were given a total dose of less than 40,000 units of dextran sulfate combined with oral administration of ethyl biscoumacetate or phenindione, and 60 patients received intravenous injections of heparin combined with oral administration of ethyl biscoumacetate or phenindione. Severe alopecia occurred in 8 of the 15 patients treated with dextran sulfate alone. It was first noticed 3 to 8 weeks after discontinuation of the treatment. Mild loss of hair occurred in 2 of the 12 patients who received combined treatment with dextran sulfate and coumarin preparations. Of the 60 patients treated with heparin and a coumarin preparation, 3 reported mild or moderate loss of hair after therapy. Mild diarrhea and depression of the platelet count were also noted in 3 of the 8 patients with severe alopecia. Severe diarrhea with loss of blood in the stools occurred in 2 other patients who had received total doses of 140,000 and 185,000 units of dextran sulfate.

A review of the literature showed that dextran sulfate therapy has been previously reported to be followed by alopecia in 10% of the patients treated. There have been several accounts of alopecia occurring as a toxic effect of heparin, but estimates of the frequency of this complication have varied greatly. The high incidence of alopecia, the occurrence of severe diarrhea in some patients, and the possibility of a profound reduction in platelets in at least a few patients make treatment with dextran sulfate in high doses clearly undesirable. Administration of 5,000 units of dextran sulfate intravenously every 8 hours for 24 to 48 hours appears suitable as an alternative to the administration of heparin to cover the period until oral administration of an anticoagulant becomes effective. The mechanism by which dextran sulfate produces its effect on hair growth is unknown.

Osteoarthritis of the Knee: Treatment by Local Injection of Salicylate Compounds. K. A. Ross, J. H. Mayer and M. M. Shepherd. Brit. M. J. 1:1040-1043 (May 3) 1958 [London].

Twelve men and 41 women, between the ages of 34 and 79 years, with osteoarthritis of the knee were treated by intra-articular injections of benzyl salicylate in oil, given at weekly intervals for 6 weeks. The number of knees treated in these 53 patients was 88. Eighteen knees received an intraosseous injection in addition to the 6-week course, and 1 patient who had both knees treated had the 6-week course and 2 intraosseous injections. The method used in these patients was devised by G. L. Scott; 0.1 to 0.3 cc. of a solution of 5% benzyl salicylate, 5% camphor, and 100% of peanut oil was employed for the intra-articular injections, and 50 to 80 cc. of a solution of 0.2% of salicylic acid, 1% of sodium citrate, 0.5% chlorbutol, 0.2% phenol red, and 100% distilled water was employed for the intraosseous injections, the dose being divided between the femur and the tibia. The clinical results in the 88 knees were analyzed by an assessor not concerned with either the selection of patients or their treatment.

The results were excellent in 24 knees, good in 27, fair in 16, and poor in 21, taking into account as criteria pain, function by performance, physical signs, and the patient's own assessment. Sodium salicylate and acetylsalicylic acid inhibit the release of histamine and similar substances resulting from tissue breakdown which may play a part in the production of symptoms in osteoarthritis. Local injection produces a high concentration of the salicylate at the point where its action is required. The intraosseous injection probably acts both generally and locally. The treatment itself is not pleasant, causing a temporary exacerbation of local symptoms and also considerable general malaise in many cases. If this is borne in mind, it is of significance that 35 patients classified themselves as "enthusiastically pleased" and 29 as "pleased" by the result of the treatment. The clinical results obtained justify further investigation of this method.

Clinical Experiences with New Cytostatic Agents in Malignant Disease. N. J. Perevodtchikova. German M. Month. 3:104-107 (April) 1958 (In English) [Stuttgart, Germany].

Two new chloroethylamine compounds, Sarkolysin [DL-*p* (bis-[beta-chloro-ethyl]-amino) phenylalanine-hydrochloride] and Dopan[4-methyl-5-(bis-[beta-chloro-ethyl]-amino)-uracil], were used in the treatment of patients with malignant disease at the Institute of Experimental Cancer Pathology and Treatment of the Academy of Medical Sciences in Moscow, U.S.S.R. Sarkolysin was given a therapeutic trial in 143 patients with inoperable metastasizing neoplasms. A 0.25% solution of Sarkolysin in isotonic sodium chloride solution was administered intravenously, intra-arterially, or orally according to the nature and location of the tumor. The drug was given once a week in doses of 40 to 50 mg., with a total dose of 200 to 250 mg. Seminoma and particularly its metastases, reticulosarcoma, Ewing's sarcoma, malignant endothelioma, primary tumors of the liver and biliary tract, thymoma, and multiple myeloma were found to be susceptible to the action of Sarkolysin. Best results were obtained in patients with seminoma; 19 of 23 patients with grade 4 seminoma responded favorably, with considerable reduction in the size of the metastases in 8 and with retrogression of the metastases in 11; in none of the 23 patients did the tumor disappear completely. Frequent blood examinations are essential in the course of therapy, as Sarkolysin inhibits hematopoiesis, and leukopenia and thrombocytopenia may occur. Excessive doses may produce granulocytopenia. It is advisable to discontinue the administration of Sarkolysin, if the leukocyte count drops below 3,000 per cubic millimeter and the platelet count below 100,000 per cubic millimeter. The greatest care must be exercised in the use of Sarkolysin in patients who have previously received radiotherapy. Sarkolysin is a suitable cytostatic agent for the combined treatment of a variety of tumors, particularly seminoma.

Dopan, the cytostatic spectrum of which corresponds to that of chloroethylamine, was given orally in doses of 10 mg. at intervals of 4 or 5 days, with a total dose of no more than 50 to 80 mg. It proved effective almost exclusively against chronic granulocytic leukemia and Hodgkin's disease. Of 61 patients with Hodgkin's disease, 41 responded favorably to the drug; in 5 of these, the enlarged peripheral and mediastinal lymph nodes were restored to their normal size, pruritus disappeared, and the temperature was restored to normal. Improvement in general condition occurred in 36 patients, with temperature restored to normal and disappearance of pruritus; the lymph nodes which had formed large masses became separated and diminished in size. Thirteen of the 41 patients had recurrences after 1½ to 9 months. Leukopenia and thrombocytopenia occurred as side-effects, but gastrointestinal disturbances were rare and mild. Dopan is the drug of choice in the treatment of Hodgkin's disease.

Treatment of Vascular Diseases with Hormones: Clinical Experiences. F. Tvedegaard. Ugesk. læger 120:527-532 (April 24) 1958 (In Danish) [Copenhagen].

Tvedegaard finds that sexual hormones and the pancreatic sterone "padutin" have an undoubted effect on the circulation and are especially curative in vascular diseases, such as endangiitis obliterans and arteriosclerosis. He concludes that these disorders are mainly due to lowered or terminated function of the endocrine glands which produce the hormones, and the treatment must be constant administration of a sufficient amount of the lacking substance.

The Use of Radioactive Phosphorus in the Therapy of Leukemia, Polycythemia Vera and Lymphomas: A Report of 10 Years' Experience. R. B. Chodos and J. F. Ross. Ann. Int. Med. 48:956-977 (May) 1958 [Lancaster, Pa.].

Radioactive phosphorus (P^{32}) therapy was given at the Massachusetts Memorial Hospital, Boston, to 71 patients between 1944 and 1952; 30 of these patients had chronic granulocytic leukemia, 12 had chronic lymphocytic leukemia, 7 had polycythemia vera, 7 had multiple myeloma, 4 had Hodgkin's disease, 8 had acute leukemia, 1 had chronic monocytic leukemia, and 2 had mycosis fungoides. P^{32} was administered intravenously as an aqueous solution of sodium phosphate. The quantity of P^{32} given varied and was dependent on the disease being treated, its severity, and the response of the individual patient. No effort was made to calculate the dose precisely on the basis of the patient's weight, although this factor was taken into consideration. A larger initial course was usually employed in patients with chronic granulocytic leukemia (10 to 12 mc.) than in those with chronic lymphocytic leukemia (6 to 8 mc.). P^{32} was administered usually in doses of 1 to 4 mc. at 1-to-7-day intervals. After the institution of the treatment, the patients were evaluated at intervals of from 1 to 2 months. If there was evidence of progression of their disease, doses of 1 to 5 mc. of P^{32} were given in an effort to maintain the leukocyte count in the range of 15,000 to 30,000 per cubic millimeter and the patient in clinical remission.

P^{32} appeared to be of significant benefit in the management of 27 of the 30 patients with chronic granulocytic leukemia and of transient benefit in the remaining 3 patients; leukopenia, thrombocytopenia, and terminal blastic leukemia were observed after P^{32} therapy. P^{32} was of significant benefit in 5 of the 12 patients with chronic lymphocytic leukemia, of limited benefit in 3, of transient benefit in 2, and of no benefit in 2. P^{32} controlled the polycythemic process from 1 to 5 years in the 7 patients with polycythemia vera; a terminal leukemia occurred in one of these patients, and a refractory anemia in another; leukopenia occurred in 3 patients, and mild thrombocytopenia in 4; hemorrhagic and thrombotic complications were mild and occurred infrequently. The treatment was not of any significant benefit in the patients with Hodgkin's disease, multiple myeloma, acute leukemia, and mycosis fungoides.

The advantages of P^{32} therapy include ease of administration, infrequency of radiation sickness, and the fact that it can be given with minimal inconvenience to the patient. Patients treated with P^{32} survive approximately as long as those treated with other agents. However, the survival of patients in this group who were treated intermittently with P^{32} was significantly less than that obtained by Osgood with continuous titrated irradiation. Supplementary roentgen-ray therapy was used, if needed, to reduce splenomegaly or lymphadenopathy. Supportive therapy with blood transfusions and administration of antibiotics and steroids was used as required. Leukopenia, thrombocytopenia, acute blastic leukemia, and terminal anemia are the hazards of P^{32} therapy, which must be considered whenever this agent is administered.

Perforation and Hemorrhage from Duodenal Ulcer During the Administration of Rauwolfia Serpentina: Report of Five Cases. W. O. West. Ann. Int. Med. 48:1033-1039 (May) 1958 [Lancaster, Pa.].

Of 42 patients with perforation and hemorrhage from duodenal ulcer observed in the course of the last 1½ years at the Charleston Memorial Hospital in Charleston, W. Va., 5 (12%) were taking drugs prepared from Rauwolfia serpentina for hypertension when the complications occurred. This was thought to represent a cause-and-effect relationship. The 5 patients included 4 men and 1 woman, all of whom were over 50 years of age, and 4 gave a fairly definite history of peptic ulcer. Rauwolfia preparations should not be given to patients with peptic ulcer. If such a preparation as Reserpine or Raudixin is employed, the potential rise in gastric acidity should be buffered with antacids or between-meal feedings prophylactically. Anticholinergic drugs are probably of little value. If vague or specific upper gastrointestinal symptoms occur in the course of treatment with a Rauwolfia alkaloid, administration of the agent should be discontinued, and the patient evaluated clinically and, if possible, by roentgenologic examination. In patients from whom an adequate history cannot be obtained or in those who cannot communicate their feelings, another antihypertensive drug or a tranquilizer, if indicated, should be employed. Mild, labile essential hypertension is best treated by sedation with phenobarbital, low-salt diet, and weight reduction if the patient is overweight. The occurrence and recurrence of peptic ulcer and its complications associated with the administration of Rauwolfia preparations probably are to be considered as another addition to the ever-growing list of "diseases of medical progress."

PATHOLOGY

The Gastric and Jejunal Mucosae in Healthy Patients with Partial Gastrectomy. F. Lees and L. C. Grandjean. A. M. A. Arch. Int. Med. 101:943-951 (May) 1958 [Chicago].

In the belief that the gastric and jejunal mucosae may help to throw light on some of the postgastrectomy syndromes, the authors present the results of 41 biopsies done with a suction biopsy tube. The patients had been requested to attend the outpatient clinic, and they were asked if they would volunteer for gastric biopsy. A completely unbiased analysis of symptoms was recorded before the results of biopsy were known. The 41 patients could be considered "normal" or healthy. They had no anemia and no gastrointestinal symptoms, apart from mild postprandial discomfort after large meals or after eating certain foods which they had learned to avoid. These minor symptoms might be considered to be "normal" after partial gastrectomy. All those who had severe symptoms after meals, recognizable dumping syndromes, anemia, diarrhea, weight loss, anorexia, or pain were excluded from this survey. Specimens of gastric mucosa were obtained from 33 of the 41 patients, and jejunal specimens from 8 patients.

The gastric musoca proved to be normal in only 1 of the patients, a man, aged 41 years, who had been subjected to a Billroth type 1 gastrectomy for duodenal ulcer. Ten patients had slight changes in the gastric mucosa, consisting of 1 or more of the following features: an irregular surface layer of cells, distortion of the gland foveolas, and moderate superficial infiltration with plasma cells, lymphocytes, or polymorphonuclear neutrophils. Some also had lymphocyte aggregations. No atrophy was present. All 10 had had a Polya type gastrectomy. Twenty-two patients had severe abnormalities in the gastric mucosa. All those with severe changes had some degree of atrophy. Pseudopyloric glands were associated with very severe changes. Those who had dilated glands lined with flat epithelium could be described as having "cystic gastritis." Flattened or distorted cells on the surface of the mucosa tended to occur in the more abnormal group of cases. This also applies to gross corkscrewing of the foveolas. The more severe abnormalities seemed to occur mostly in older patients. The specimens of the jejunal mucosa were essentially normal in appearance.

The authors suggest that these findings may be useful for comparison with various types of postgastrectomy syndromes. It cannot be assumed that musocal disease is the cause of symptoms. A completely atrophic mucosa may be found in the patient in whom pernicious anemia is liable to develop at a later date; it is unlikely to be found in a patient with anastomotic ulceration because of lack of acid secretion. Even a moderate atrophy might protect the patient from anastomotic ulceration—in this case one might consider that atrophy is desirable. Severe gastritis with or without atrophy in the stump does not cause symptoms which disturb the patient unduly, but these patients are accustomed to slight symptoms, which they learn to ignore, and, therefore, one cannot conclude from this study that such gastritis would not cause symptoms in others.

In an addendum it is stated that suction biopsy in 4 patients with postgastrectomy syndromes, who had anastomotic ulceration and bleeding, revealed no mucosal atrophy at all. Of 4 patients thought to have iron-deficiency anemia without ulceration, 2 had moderate atrophy and 2 had none. One patient with steatorrhea had slight atrophy, and another had complete atrophy. Three with dumping syndromes, alone showed slight and moderate atrophy. All showed excessive inflammatory infiltration. Many more cases must be studied before a proper assessment can be made.

Pulmonary Aspergillosis. D. Fernández Luna. Rev. brasil. tuberc. 26:1-14 (April) 1958 (In Spanish) [Rio de Janeiro].

A man, 27 years old, died as a result of cor pulmonale complicating a pulmonary disease of long duration. A diagnosis of bilateral pulmonary tuberculosis with cavitation had been made. An autopsy confirmed the diagnosis. Histological examination of pulmonary tissue was negative for tubercle bacilli. One cavity, which was different from the others, appeared macroscopically as if it were a large blood coagulum of long standing. Histologically this cavity was an intracavitary aspergilloma containing fungi in large number and simulating a trichobezoar. Pulmonary aspergillosis has become more frequent since the discovery of antibiotics. Its frequency is linked to an abuse of antibiotics. Pulmonary aspergilloma shows a roentgenologic picture similar to that of pulmonary hydatidosis. Pulmonary aspergillosis may be secondary to chronic pulmonary tuberculosis, which regresses as soon as pulmonary aspergillosis develops, showing an antagonism between the fungi and the tubercle bacilli.

Duodenal and Gastric Ulcer in Childhood and in Adolescence. M. Tinti, F. Terreni and E. Taddeucci. Sett. med. 45:629-640 (Dec. 15) 1957 (In Italian) [Florence, Italy].

The authors report on 10 boys and 1 girl with duodenal ulcer; 2 were aged 7 and 10 years, and 9 ranged in age from 14 to 25. There was no history of neonatal type of this disease or of gastric ulcer. Three patients had had ulcerous disorders associated with cerebral disease since infancy. The ulcers tended to be chronic since the inception of the disease. The hereditary element of the disease was present in more than half of the patients. Good clinical results were obtained in all the patients, including 2 who underwent operation after a prolonged waiting period.

The authors believe that ulcerative lesion may manifest itself either in the stomach or in the duodenum, whereas ulcer disease has predilection for the duodenum and for the male sex. Gastric ulcer and duodenal ulcer are from the early years of life 2 distinct diseases, although they have the same morphologic characteristics. Duodenal ulcer is the protopathic feature of ulcer disease and not of ulcerative lesion. Gastric ulcer seems to be a secondary pathological manifestation, symptomatic, tardive, and not necessarily fitting into the description of ulcer disease; this is evident by observing the development of the disease in patients during the first years of life and becomes more clearly so in adulthood.

Gastric Ulcer and Duodenal Ulcer in the Aged. M. Tinti, F. Terreni and E. Taddeucci. Sett. med. 45:662-669 (Dec. 31) 1957 (In Italian) [Florence, Italy].

The authors discuss the incidence of gastric ulcer and of duodenal ulcer in 128 patients over 50 years of age. This study includes 36 patients with gastric ulcer and 13 patients with duodenal ulcer in whom the first clinical signs of the disease appeared when they were past 50, and 79 patients in whom the disease appeared earlier. The ratio of gastric ulcer to duodenal ulcer in the aged was 3:1, and the ratio of both types with respect to men and women was 2:1. Gastric ulcer in the aged was localized in the small curvature and consisted of a single lesion; multiple lesions were present in only 1 patient. The lesions varied in size from small to medium. Surface lesions of ulcer in the aged were observed in about half of the patients; deeper lesions which penetrated to, or beyond the tunica serosa, were observed in the others.

The authors believe that gastric ulcer and duodenal ulcer are 2 separate clinical entities, with different etiology, pathogenesis, and clinical signs. Ordinarily ulcer disease manifests itself mostly as duodenal ulcer; gastric ulcer is related to local rather than to systemic conditions. Ulcer in the aged can be regarded as manifestation of a local, elective arteriosclerosis, which affects persons congenitally predisposed to it. The disease belongs to the broader class of arteriosclerosis. For the formation of ulcer in the aged, congenital predisposition must be associated with the existence either of an elective, local pathological lesion, such as arteriosclerosis, or of additional elements of general nature, such as emotion (war ulcers).

Serum Transaminase: The Diagnostic Value of the Estimation in Cardiac Infarction and Liver Damage. N. M. Gutteridge and C. J. McKean. M. J. Australia 1:528-535 (April 19) 1958 [Sydney].

Glutamic oxaloacetic transaminase is abundant in many animal tissues. The enzyme has been found in all normal serums. The highest concentrations are found in heart muscle, skeletal muscle, brain, liver, and kidney, in that decreasing order. If a significant cell damage or destruction occurs in any of these tissues, the enzyme is liberated from the damaged cells into the blood, with a resultant rise in serum glutamic oxaloacetic transaminase (SGO-T) level. The authors review 4 available methods for the assay of the SGO-T level, namely, the chromatographic method of Karmen, La Due, and Wroblewski, the spectrophotometric method of Karmen, the colorimetric method of Umbreit and Cabaud, and the colorimetric method developed by Reitman and Frankel, which is known also as the Sigma-Frankel method. The advantages of this last method are emphasized. One hundred university students and laboratory personnel were tested with the Sigma-Frankel colorimetric method to establish a normal range for SGO-T activity. Values ranged from 6 to 32 units, with mean activity of 14 units, and standard deviation of ± 5.7 units. The results were unaffected by age, sex, fasting state, muscular exercise, or minor pathological state. SGO-T levels in various disease states not involving acute damage of heart muscle, skeletal muscle, or liver tissue were within the normal range, with the exception of acute pancreatitis which was associated with an increased level.

The SGO-T level rose to 2 to 20 times the normal level within 12 to 24 hours after acute myocardial infarction, and returned to the normal range within 3 to 7 days. The authors briefly describe several patients in whom they suspected myocardial infarction, and they cite the results obtained in various cardiac conditions by several investigators. In suspected myocardial infarction the SGO-T assay corrects and supplements the diagnostic inadequacies of the electrocardiogram, the erythrocyte sedimentation rate, and the leukocyte count. The transient myocardial ischemia of angina pectoris is not accompanied by an elevation of the SGO-T level; thus, serial SGO-T assay will differentiate myocardial infarction and angina when electrocardiographic evidence is not conclusive. SGO-T values tend to be diagnostic of myocardial infarction before a definite electrocardiogram is available. Elevated SGO-T values will clarify an electrocardiographic diagnostic problem when a left bundle-branch block or the effects of digitalis obscure the tracing. SGO-T assays will help differentiate a recent myocardial infarct from acute pericarditis, and a recent infarct superimposed on an old one. SGO-T assays can aid the differential diagnosis between pulmonary thrombosis and myocardial infarction in cases of acute thoracic pain in the postoperative period. The SGO-T level is not increased in pulmonary thrombosis. The peak SGO-T value reached after infarction is roughly proportional to the size of the infarct. Serial assays will thus make it possible to gauge the amount of heart muscle damage. Very high SGO-T levels after infarction are associated with a bad prognosis. A single SGO-T assay after 24 hours can be valuable, but it is advisable to make an assay every 12 hours for the first 2 or 3 days after infarction.

Serial SGO-T estimations are valuable also in the differential diagnosis of acute and chronic hepatic disease, and in the management of acute hepatitis, with regard to the effectiveness of treatment, the correct time for ambulation, the detection of relapses before the onset of clinical symptoms, and the prognosis. Other possible uses, as a sensitive index of liver-cell injury, are (1) for the control of the dosage of potentially hepatotoxic drugs and (2) for the control of endemic and epidemic hepatitis.

X **Hepatitis Complicated by Manifestations of Lupus Erythematosus.** L. I. Taft, I. R. Mackay and L. Larkin. J. Path. & Bact. 75:399-404 (April) 1958 [Edinburgh].

The factors are unknown that determine the progression of acute hepatitis to the chronic stage, particularly in cases with a relatively mild initial illness. The possibility that autoimmunological factors may operate in certain of these cases was suggested by observers who emphasized the presence of some of the features of disseminated lupus erythematosus in 7 such cases. The presence of complement-fixing antibodies to human tissue antigens has been demonstrated in the serum of patients with disseminated lupus erthematosus, active chronic hepatitis, and certain other diseases. The present paper reports clinical, pathological, and complement-fixing antibody studies carried out on a patient with chronic hepatitis associated with demonstrable lupus erythematosus (L. E.) cells, glomerulonephritis, and colitis, who died after an illness of 3 years.

The patient was a 20-year-old woman. In the absence of any specific test for infection by the hepatitis virus, the initial diagnosis of this condition depended on the clinical evidence and biopsy findings. The hepatic lesion dominated the clinical and pathological course of the disease throughout and was identical with that seen in chronic infectious hepatitis. The associated lesions in the kidney and the colon were not commensurate with those in the liver, although their onset undoubtedly had an adverse effect on the disease process. In the later stages of her illness this patient was suffering from what has been termed lupoid hepatitis, that is, chronic hepatitis associated with a positive L. E.-cell test, a condition closely resembling and possibly identical with disseminated lupus erythematosus itself. However, this case of lupoid hepatitis differed from classical disseminated lupus erythematosus in certain respects: few rather than many organs were involved; the L. E.-cell test, usually consistently positive in disseminated lupus erythematosus, was only temporarily positive in this patient and was negative during the development of the glomerulonephritis and the colitis. The elevated complement-fixing antibody titers in this patient's serum supported the postulated relationship between chronic viral hepatitis, lupoid hepatitis, and disseminated lupus erythematosus.

The Osgood-Schlatter Lesion: A Radiological and Histological Study. B. Cohen and R. W. Wilkinson. Am. J. Surg. 95:731-742 (May) 1958 [New York].

Opinions are about equally divided on the etiology of Osgood-Schlatter disease (a lesion of the tuberosity of the tibia). Some favor a traumatic basis, while others feel that the disease is allied to the osteochondroses. Radiologic descriptions have tended to be influenced by the osteochondritic theory. Opportunities for histological examination have been few. The authors observed 12 patients with this disorder, of whom 7 were boys and 5 were girls. The records of 11 patients are presented. Nine patients, 4 girls and 5 boys, underwent operative removal of the tubercles, 1 of the boys having both tubercles removed. In 7 patients histological examination of the tubercle was possible. On the basis of this study the authors believe that there is no justification for regarding this condition as an aseptic necrosis of bone, nor should it be grouped with the osteochondroses. The distinctive features emerging from radiologic and histological examination suggest that this condition is essentially the result of a dislocation of appositional structures within the tibial tubercle complex, that this dislocation is not preceded by underlying disease, that it is followed by repair reactions, and that its origin can most feasibly be ascribed to trauma. The authors consider the term "Osgood-Schlatter disease" a misnomer. If the eponym is to be preserved, "Osgood-Schlatter lesion" would be a more accurate term and less misleading.

Carcinoma and Ulcerative Colitis: A Clinical-Pathologic Study: II. Statistical Analysis. M. B. Goldgraber, E. M. Humphreys, J. B. Kirsner and W. L. Palmer. Gastroenterology 34:840-846 (May) 1958 [Baltimore].

Fourteen of 86 deceased patients with ulcerative colitis had carcinoma of the intestine, a frequency of 16.2%. A comparison of the group of 86 patients with other groups of the same race, sex, and age in the population at large has shown a ninefold increase in frequency of death from colonic cancer. There has been a fourfold increase in frequency of death from rectal cancer, other things being equal. The over-all increase in frequency is eightfold. Although three times as many deaths occur from cancer of the breast as from colonic cancer in women of the age groups of this series, only 1 death from breast cancer was observed as compared with 9 from colonic and rectal cancers, a reversal of the expected cancer-death pattern. Rectal cancer accounts for about one-third of intestinal cancers; rectal cancer deaths constitute from 37 to 45% of the deaths from colonic cancer. Only 2 of the authors' patients died of rectal cancer, as compared with 12 who died of colonic cancer.

Fibroelastosis of the Endocardium. E. Boye. Ugesk. læger 120:445-447 (April 3) 1958 (In Danish) [Copenhagen].

Fibroelastosis of the endocardium is a congenital heart disease characterized by an increase in the fibroelastic tissue of the endocardium; it is most frequently accompanied by hypertrophy of the heart musculature and generally by other anomalies of the heart. Diagnosis can be made only at autopsy. There is no causal treatment. In the 2 cases described, the symptoms set in shortly after birth. Death occurred when the infants were 7 and 11 weeks old respectively. In both instances autopsy revealed typical gray-white changes in the endocardium and hypertrophy of the heart musculature. In the first case there were also marked changes in the aortic valves and persistent ductus arteriosus. The second case was without other congenital malformations.

PHYSIOLOGY

Potassium Metabolism and Renal Function. T. Hilden. Ugesk. læger 120:468-471 (April 10) 1958 (In Danish) [Copenhagen].

Attention is called to the marked interaction between renal function and potassium metabolism. Acquaintance with this can help to illuminate the often complicated biochemical disturbances which may occur on changes in the renal function and disturbances in the potassium metabolism. Hyperpotassemia, mainly seen in grave, acute, or chronic renal injuries, leads to such pronounced changes in the function of the muscle-nerve system and to so pronounced an effect on the myocardium that the outcome is often fatal if the potassium concentration in the serum is not reduced. Hypopotassemia is more frequent and often of longer duration or chronic. Potassium deficiency entails a reduction in the glomerulus filtration and in the tubular *p*-aminohippuric acid secretion. The distal tubulus function is changed even on moderate potassium deficiency. Deficient concentration ability is characteristic and leads to polyuria. Correction of the potassium deficiency rapidly restores the renal ability to secrete concentrated urine. Continued vomiting of acid gastric contents means a certain potassium loss for the organism. The alkalosis due to the loss of acid promotes potassium excretion through the kidneys. Because of the effect of the gradual potassium deficiency on the renal function, excretion of an alkaline urine becomes impossible. The vicious circle can be broken only by the administration of potassium salts. On overproduction of mineral corticoids or on treatment with hormones of the adrenal cortex, the increased elimination of potassium can cause a general potassium deficiency in the organism. At the same time there is an alkalosis explained by the increased hydrogen ion elimination due to the potassium deficiency. Hypochloremia and increased serum bicarbonate result.

On the Fat-Mobilising Activity of Human Urine. T. M. Chalmers, A. Kekwick and G. L. S. Pawan. Lancet 1:866-869 (April 26) 1958 [London].

Previous studies on obese persons had demonstrated that, if the calorie content of the diet is kept constant, the rate of weight loss varies considerably with alterations in the composition of the diet. Evidence was also obtained to suggest that the decrease in body weight could be accounted for by loss of body fat and water. It appeared that a mechanism existed for controlling the mobilization of depot fat, which must be sensitive to changes in the composition as well as the calorie content of the diet. Such a mechanism should be operating at its maximum during fasting, and if any hormonal agent were involved, it should be detectable in the urine. The authors describe experiments they carried out to determine the effect on fat metabolism of urine collected from healthy persons during periods of fasting which lasted 36 hours, the urine being collected during the last 24 hours of these periods. The batches of urine were then extracted, and the extracts were injected into mice. It was found that a substance or complex is present in the urine of healthy, fasting subjects and that, on injection into mice, this substance (1) increases the total amount of fat in the liver, (2) mobilizes fat from the fat depots, (3) appears to increase the total metabolic turnover of fat in the animals, and (4) causes weight loss without depressing appetite when given over a period of time, the loss being in the form of body fat and water.

The active material has been partially purified by paper chromatography. However, the substance or complex cannot be detected in identical extracts made from the urine of healthy subjects when they are on a normal mixed diet rather than fasting. The substance (called here fat-mobilizing substance) seems to be present in the urine in conditions other than fasting which are associated with weight loss, such as that in patients with malignant disease. Studies on 3 obese patients revealed that weight loss was greatest when the calories were given mainly in the form of fat; losses were smaller with high-protein diets. When carbohydrate made up the major part of the calorie intake, little or no weight was lost.

PUBLIC HEALTH

A Study of Illness in a Group of Cleveland Families: Acquisition of Type-Specific Adenovirus Antibodies in the First Five Years of Life—Implications for the Use of Adenovirus Vaccine. W. S. Jordan Jr., G. F. Badger and J. H. Dingle. New England J. Med. 258:1041-1044 (May 22) 1958 [Boston].

Adenovirus antibodies are common in civilian populations, and yet these viruses cause only 0.5 to 3% of the respiratory illnesses among families, college students, and adults. Clinical adenovirus infections may be uncommon in the groups studied, because in many of the patients immunity had already developed as a result of such infections earlier in life. Indeed, by the age of 5 years, more than 80% of children have antibody to at least 1 type, and approximately 50% have antibodies to 2 or more types. If the major burden of adenovirus disease in civilian life is borne by infants and young children, it is important to determine when the infections occur and whether or not prevention should be attempted through immunization of children.

Serial serum specimens collected from birth to 5 years of age from children in a population of Cleveland families under constant observation were tested for neutralizing adenovirus antibodies. Maternal adenovirus antibodies were freely transferred across the placenta, but at 6 months of age most children had no adenovirus antibody. As measured by antibody acquisition, type 1 and type 2 infections were common during the first 5 years of life. By the age of 5 years the percentage of children with types 1, 2, and 6 antibodies was the same as that in the adult group. Infections due to types 3, 5, and 7 were relatively infrequent, the prevalence of the different antibodies at age 5 being about half of the adult level. It is concluded that the generalized use of adenovirus vaccine in civilian populations is not warranted at present.

The Evanston Dental Caries Study: XVIII. Report on the Permanent Teeth Dental Caries Experience Rate of the Children in the Control Area (Oak Park, Illinois). I. N. Hill, J. R. Blayney and W. Wolf. J. Am. Dent. A. 56:688-691 (May) 1958 [Chicago].

Water fluoridation was begun in Oak Park, Ill., in August, 1956. Since this village had been selected as a control area for ascertaining the effects of fluoridation in Evanston, Ill., dental examinations of Oak Park children were repeated in January, 1956, rather than in 1958 as had been planned originally. The authors compare the permanent teeth dental caries rates of 2,051 children, 6, 7, 8, 12, 13, and 14 years of age, examined in the control fluorine-free area (Oak Park) in 1947, with the results of 2,537 dental examinations made 9 years later in the same area. Evanston and Oak Park have a similar economic level and participate in comparable educational programs. Therefore, any change in the dental caries rate between the first (1947) and the second (1956) study in Oak Park would be applicable to Evanston, and, if these changes were significant, it would be necessary to adjust the Evanston figures accordingly. Over the 9-year period the authors found no significant change in the caries prevalence rates in children who were 6, 8, 12, 13, and 14 years old. They did note a significant increase in the prevalence rate in the 7-year-old children. Since the control area showed no statistically significant change in the dental caries experience rates over a 9-year period, no adjustment was made in the Evanston rates. It is concluded that the reduction in the dental caries experience rates of the children of the study area (Evanston) is due solely to the sodium fluoride in the Evanston water.

BOOK REVIEWS

Glaucoma: Transactions of the Second Conference, December 3, 4, and 5, 1956, Princeton, N. J. Edited by Frank W. Newell, M.D. Sponsored by Josiah Macy, Jr. Foundation. Cloth. $4.95. Pp. 245, with 63 illustrations. The Foundation, 16 W. 46th St., New York 36, 1957.

The conference here reported dealt with the mechanisms of the formation of the aqueous humor, mathematical formulation of aqueous humor dynamics, mechanisms of transport by membranes, and applanation tonometry. The 25 participants gave their "off-the-cuff" opinions informally. The exchange of ideas served to promote effective communication across departmental walls which so often tend to isolate the professions and specialists from one another. Goldmann emphasized important diagnostic criteria in differentiating the findings in severe myopia and those of glaucoma in the same eye. He pointed out that when one measures the distance between the lamina cribrosa sclerae and retina above or below the papilla he finds that the distance is smaller in the glaucomatous myopic eye than it is in the normal eye—about half the normal distance: the average distance in normal eyes is 0.72 mm., and in glaucomatous myopic eyes it is 0.39 mm. His discussion of applanation tonometry is exceedingly enlightening and is recommended for all ophthalmologists who desire to understand the glaucoma problem. This book is being sold at cost.

The Handicapped and Their Rehabilitation. Edited by Harry A. Pattison, M.D., F.A.C.P. Introduction by Major General Melvin J. Maas. Cloth. $14.75. Pp. 944, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1957.

This volume is basically a reference work consisting of a series of essays by 44 authorities in the field of rehabilitation. Its primary purpose is the orientation of the different members of the rehabilitation team regarding the contributions which different members of this team may make and the widely varied problems which may have to be considered in the rehabilitation of the patient. The book is divided into four parts. The first gives the general principles and philosophy of rehabilitation. The opening chapter, by Dr. A. B. C. Knudsen, outlines the scope of rehabilitation and gives in some detail the development and organization of the rehabilitation services of the Veterans Administration. A second chapter by Dr. Pattison considers philosophically the relationship of the physical and mental constitution of the patient to the rehabilitation program. He points out that the success or failure of the rehabilitation program in the individual patient is as dependent on the individual as it is on the services offered to him. The second part deals with nontraumatic disabilities, plastic and reconstructive surgery, cardiac disease, tuberculosis, the injured worker, the elderly person, the physically handicapped child, the blind, the hard-of-hearing, the patient with cancer, the diabetic, the epileptic, and the psychiatric patient. The chapter by Dr. Morton Hoberman, dealing with the rehabilitation of the physically handicapped child, is particularly commendable, as are those chapters dealing with geriatrics, blindness, the hard-of-hearing, and the epileptic. The chapter on plastic and reconstructive surgery, although good as a surgical treatise, seems too technical for a book of this type and more appropriate for a textbook of surgery. The chapters dealing with cardiac diseases and psychiatric conditions provide a good orientation to these problems for the auxiliary workers in the field of rehabilitation, such as therapists and counselors, but offer little that is new to physicians.

The third section presents in detail the historical development and the possible current functions of the many professions and services which may be represented on the rehabilitation team. The personnel include the medical rehabilitation coordinator, the medical social worker, the rehabilitation nurse, the occupational therapist, the vocational rehabilitation counselor, the physical therapist, the corrective therapist, the educational therapist, the manual arts therapist, the librarian, the music therapist, the psychologist, the psychiatrist, and the clergyman. The newest member of this team to have been added in some rehabilitation centers is the medical rehabilitation coordinator, a layman who is supposed to be a professional co-worker with the chief. The office developed from that of an administrative worker who could take care of nonmedical administrative problems in the rehabilitation center. Nowadays, the coordinator appears to have a tendency to preempt some duties which are properly those of the physician, such as being certain that the patient is receiving all of the therapeutic services his problems justify. The fourth section deals with special problems and procedures in rehabilitation. This is a heterogenous group of essays concerned with fatigue, nutrition, the education of patients and their families in better home economics, the sheltered workshop, placement in industry, workmen's compensation, the attitudes of organized labor toward rehabilitation, and the extensive state-federal program of vocational rehabilitation. The book covers a wide range of topics and

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

presents an interesting review of the recent development of the more complex types of rehabilitation program. It seems, however, to imply that rehabilitation cannot be practiced properly without having available this wide diversity of special therapies, although many rehabilitation centers in the country function well with only a few of these team members or with the work which would be done by some of them being provided for the patient in other ways. The physician who is interested in the rehabilitation of patients may find many suggestions in this book to guide his thinking. It should be of value primarily as a reference book rather than as a textbook.

Psychopharmacology: Pharmacologic Effects on Behavior. Edited by Harry H. Pennes, M.D., D. Med.Sci. (Neurology). With 41 participants. [Volume III] Progress in Neurobiology. Series editors: Saul R. Korey, M.D., Professor of Medicine (Neurology), Albert Einstein College of Medicine of Yeshiva University, New York, and John I. Nurnberger, M.D., Chairman and Professor, Department of Psychiatry, Indiana University School of Medicine, Indianapolis. Cloth. $8. Pp. 362, with 35 illustrations. Paul B. Hoeber, Inc. (medical book department of Harper & Brothers), 49 E. 33rd St., New York 16, 1958.

In the comparatively short period since the clinical introduction of the so-called tranquilizing drugs, the number of workers and the volume of literature in the field of psychopharmacology have expanded at prodigious rates. Much of this work has been devoted to clinical evaluation of new drugs, an effort that has been vastly rewarding despite the general empirical nature of the investigations. The major emphasis of the laboratory studies has been directed toward an elucidation of the basic mechanisms whereby chemical compounds can act on biological systems in such a manner as selectively to influence mental behavior. Many approaches to this highly complex problem have been explored and have resulted in the accumulation of much knowledge concerning the biochemical, pharmacological, physiological, pathological, and psychological effects of the tranquilizing drugs and the hallucinogens. This volume, probably the most ambitious work of its kind to appear to date, presents a comprehensive survey of the current status of knowledge in these areas. The 41 participants in the symposium reported on have discussed such topics as the biochemical, metabolic, and electrophysiological aspects of tranquilizing drug action, the serotonin hypothesis of psychotomimetic action, and the effect of indoles on central nervous system function. There are several excellent presentations on methodology in screening and evaluating new drugs. Included also are discussions of the psychoanalytical and clinical aspects of tranquilizing drug action. Most of the papers are followed by provocative discussions by other participants. There is an adequate subject index. Except for those portions dealing with behavioral changes after the use of tranquilizing and hallucinogenic drugs in man, most of this book is of such a highly technical nature that it will probably be beyond the scope of interest of the average physician. The book should prove to be a valuable reference source for all investigating workers in psychopharmacology, a new medical discipline which embraces biochemistry, enzymology, pharmacology, experimental psychology, and psychiatry.

The Administration of Health Education and Physical Education. By Jesse Feiring Williams, M.D., Sc.D., Clifford Lee Brownell, Ph.D., Professor and Chairman of Department of Health Education, Physical Education, and Recreation, Teachers College, Columbia University, New York, and Elmon Louis Vernier, Ed.D., Director of Health and Physical Education, Public Schools, Baltimore. Fifth edition. Cloth. $4.75. Pp. 387, with 35 illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1958.

Five editions of this book, over nearly a quarter of a century, record the senior authors' developing concept of how health education and physical education can be effectively administered in the schools of the United States. The authors state that this textbook "is planned for those who work in schools and colleges; it stresses the problems of the former and presents both information relative to the intricate administrations of the large city school system and materials which enable the beginning teacher in a rural community to plan his work more effectively. Its chief function is to be a text for men and women students of health education and physical education." The dependency of health education and physical education on each other and on other school and community interests is constantly stressed, as well as the relationship of persons to each other and to the pupils being taught. This is indicated by the four main subdivisions of the book. Under "Leadership," the authors discuss administration, personnel and staff, and the business end of health and physical education. Under "Program," they cover the curriculum and the organization of instructional materials in such related fields as athletics and special education. School health services and school environment are related to instruction. Under "Facilities," the authors describe the gymnasiums, classrooms, swimming pools, locker rooms, shower rooms, and the outdoor recreational areas. Finally, under "Community and State," they relate the school to the community, discuss the state's responsibility in these fields, consider legal factors and public relations, and suggest ways to evaluate health education and physical education. The material is practical and in accord with the customary interprofessional thinking of medicine and education on the administration of health education and physical education. It could well be used as a textbook in the professional preparation of teachers and administrators and as a reference book for educators in practice, as well as for physicians serving schools as medical advisors or members of boards of education.

Outline of Orthopaedics. By John Crawford Adams, M.D., F.R.C.S. Second edition. Cloth. $8. Pp. 428, with 301 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh, Scotland, 1958.

In the preface to the first edition of this textbook, the author states that it is intended primarily to help students who are studying for the qualifying examinations and that he hopes it will also be of help to practitioners whose work brings them into occasional contact with orthopedic problems and to physiotherapists and orthopedic nurses. The illustrations are well selected and clearly reproduced. The text is concise and easy to read. The introduction includes a brief but interesting history of orthopedics. Chapter 1 describes various clinical methods used in examining a patient and arriving at a diagnosis. Methods of nonoperative and operative treatment are briefly described. Chapter 2 discusses various deformities of joints, bones, and soft tissue and neurological disorders. Chapters 3 to 10 describe the orthopedic conditions that may affect different regions of the body. The author is the assistant editor of the *Journal of Bone and Joint Surgery*. This book is recommended to graduate students and orthopedists who hope to qualify for the American Board of Orthopaedic Surgery. Undergraduate students who are being taught the principles of diagnosis and treatment of orthopedic conditions should find this textbook most useful.

Electron Microscopic Atlas of Normal and Leukemic Human Blood. By Frank N. Low, Ph.D., Professor of Anatomy, Louisiana State University School of Medicine, New Orleans, and James A. Freeman. Cloth. $25. Pp. 347, with illustrations. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E.C. 4, England, 1958.

This is the first comprehensive book dealing with the electron microscopic appearance of normal and leukemic human blood cells. In the introduction, the technique developed by the authors is covered in detail and the general approach of the book, as well as the differences in the interpretation of the appearance of the cells under ordinary light and electron microscopy, is discussed. The appearance of normal blood cells, with magnifications ranging from 8,000 to 280,000, is described in the next section. The normal variations are described and illustrated in detail. The next five sections are devoted to a general description of the appearance of the cells, under various magnifications, in the leukemias before and during treatment. The point is made in this section that the differentiation of the various blast cells is no easier with the electron microscope than with the light microscope. The last two sections describe the plasma cells and the erythrocytes. Except for some minor areas which might be considered controversial, such as the occurrence of Auer bodies in monoblasts and the question of the transition of myeloblasts into cells of the erythrocyte series, the book is conservative and factual in approach. The style is simple and concise. The book is, for the most part, limited to a description and interpretation of the findings. The organization of the book is good; photographs are on the right side with clear letterings of the prints, and the descriptive legends are on the left. The prints are excellent in quality and reveal in great detail the fine structure of the cells. The index is complete, and each section has its own bibliography. Although it is unfortunate that the details revealed by the electron microscope are, at this time, only of academic interest and fail to help either etiologically or dynamically in the understanding of infectious diseases, all those interested in electron microscopy and ultrastructure of human blood cells should welcome this book.

Principles of General Surgical Management. By H. A. F. Dudley, F.R.C.S.E., Lecturer in Surgery, University of Edinburgh, Edinburgh. With assistance of B. C. Paton, M.R.C.P.E, I. F. MacLaren, F.R.C.S.E., I. B. Tait, F.R.C.S.E., and G. F. Murnaghan, F.R.C.S,, F.R.C.S.E. With foreword by John Bruce, C.B.E., T.D., F.R.C.S.E., Regius Professor of Clinical Surgery, University of Edinburgh. Cloth. $6.50. Pp. 203, with 68 illustrations. Williams & Wilkins Company, Mount Royal and Guilford Aves., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Place, Edinburgh 1, Scotland, 1958.

This monograph deals with patient care. The scope of this publication is beamed, primarily, to the surgical intern. Subjects covered include preparation for surgery, the recognition and management of shock, respiratory function and postoperative chest complications, antibiotics and chemotherapy in surgical practice, the care of wounds, the immediate postoperative period, the management of prolonged unconsciousness, postoperative thromboembolism, abdominal operations and their complications, the urinary tract, parenteral therapy, practical procedures, and investigative work in surgery. Line drawings, charts, tables, and diagrams are used to document and clarify statements and opinions. A short bibliography, which is primarily British, appears at the end of each chapter. The chapter dealing with simple laboratory tests is informative. Interns and residents should profit by reviewing this information at frequent intervals. The format is attractive, and the easy style makes reading this book a pleasure. This publication compares favorably with American publications dealing with the care of the patient, primarily in the preoperative and postoperative periods. The chief field of usefulness will lie with interns, residents, and candidates for specialty examinations. Although it is not a provincial publication, one would be reluctant to accept it in its entirety in all institutions. The interpretation of general surgery has been wide, including urology, thoracic surgery, injuries to the head, and other forms of trauma.

QUESTIONS AND ANSWERS

CONCURRENT IMMUNIZATIONS

To THE EDITOR:—*Please advise as to the contraindications, if any, of giving intercurrent immunizations, for instance, giving as the first injection DPT, followed in two weeks by smallpox vaccination, followed in two weeks by the first poliomyelitis injection. In addition, would this procedure cause adequate antibody formation as compared with the routine monthly injections? What is the present accepted immunization schedule?*

Parker W. Snyder, M.D., Peru, Ind.

ANSWER.—Several different immunization schedules for infants, some of which utilize concurrent or intercurrent immunizations, for diphtheria, pertussis, tetanus, smallpox, and poliomyelitis, have been used safely and successfully. Certain contraindications exist which relate primarily to the inadequate response of the very young infant to an antigenic stimulus. In the case of the triple antigen (DPT), the series of three shots makes possible the early formation of adequate antibodies. For smallpox, failures of the vaccine in very young infants have been shown to be due to interference by placentally transmitted maternal antibodies. It is advisable, therefore, to defer routine vaccination until after the infant is 5 months of age, when greater success can be expected. In the event of anticipated early exposure to smallpox, vaccination at any time from the newborn period on would be advisable. It seems reasonable to begin primary immunization against poliomyelitis as early as the second month of life. Injection of poliomyelitis vaccine may be done concurrently with that of other vaccines. It is recommended that, if the vaccine is given at the same time as another vaccine, they should be injected separately into different sites. Combined preparations of poliomyelitis vaccine and DPT may soon be approved and supplied commercially, but until then physicians should be cautioned not to mix currently available preparations of these materials for injections from the same syringe. The following schedule for routine immunizations of infants, based on the foregoing information, has been suggested by the Committee on the Control of Infectious Diseases of the American Academy of Pediatrics: 1 to 2 months of age, 0.5 cc. of DPT; 2 to 3 months of age, 0.5 cc. of DPT and 1.0 cc. of poliomyelitis vaccine; 3 to 4 months of age, 0.5 cc. of DPT and 1.0 cc. of poliomyelitis vaccine; 5 to 6 months of age, smallpox vaccination; 10 to 12 months of age, 1.0 cc. of poliomyelitis vaccine; and 16 to 18 months of age, 0.5 cc. of DPT.

WATER CHLORINATION AND HEPATITIS

To THE EDITOR:—*The U. S. Army in Korea superchlorinates the water, using a residual of 10 ppm, and makes no effort for dechlorination. This amount of chlorine is used in freezing weather because of the known effects of the decreased efficiency of chlorine under such conditions. At one station 2 ppm of chlorine may be in the tank and, due to stratification, sometimes none at the point of consumption 30 ft. away. The Army is plagued with poor water piping systems, with possible leaks and possible contamination from the fields where night soil is used for fertilization, so that at the point of consumption the residual of chlorine is 1-2 ppm. The people have been advised to boil the water when chlorine content was 1 ppm and then put it in the ice box for use later on. The U. S. Navy now has made the statement that no one can be hurt by drinking water with high chlorine content, since a person would not take much due to the objectionable taste. The Army particularly wants a high chlorine residue because of the outbreaks of infectious hepatitis. Some of its own epidemiologists state that chlorine is not effective against the virus of hepatitis. Goodman and Gilman state that a residue of 0.2 to 0.4 ppm is very effective against viruses. They also state that a residue of 10.0 ppm of chlorine is a definite gastric irritant. Please comment.* *M.D., California.*

ANSWER.—The control of infectious hepatitis virus in drinking water depends almost entirely on the disinfectant, because the virus is not eliminated or inactivated (it may be reduced in concentration) by preliminary coagulation, settling, and filtration of the water (Neefe and others, *Am. J. Pub. Health* 37:365, 1947). Dosages of chlorine that are adequate for inactivation of bacterial pathogens may not be adequate for that of the hepatitis virus, particularly if the water has a high content of unoxidized organic material (Neefe and others, *J. A. M. A.* 128:1076-1080 [Aug. 11] 1945; Bhagavan and others, *Indian J. M. Res.* 45:1, 1957). Total and free residual chlorine concentrations of 1.1 and 0.4

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ppm, respectively, after 30 minutes of contact apparently were adequate to inactivate the hepatitis virus under one set of experimental conditions. Amount of organic material, temperature, and contact periods directly affect the amount of disinfectant required. Substantially more free chlorine is also required to achieve comparable kills of Coxsackie A2 virus than is required to kill Escherichia coli cells (Clarke and Kabler, *Am. J. Hyg.* 59:119, 1954). White mice can grow to adulthood from weanlings and thrive on water containing 200 ppm of free available chlorine. Histological examinations of stained sections by microscopic methods showed no abnormality (*J. Am. Water Works A.* 48:1903, 1956). At Fort Bragg, N. C., over 150 persons used water with a chlorine content of 50 ppm. After the 1951 flood on the Kansas River, chlorine residuals of as high as 90 ppm were carried in the distribution system of North Lawrence, Kan. Residents drank the highly chlorinated water with no known adverse effects. During the Ohio River flood of 1937, 50 ppm was used in the distribution system at Golconda, Ill. No adverse reactions were reported (*J. Am. Water Works A.* 48:1057, 1956).

FIRE HAZARDS OF VAPORIZED ALCOHOL

To the Editor:—*What are the explosive and fire hazards of giving 45 to 90% alcohol bubbled through oxygen for pulmonary edema? The oxygen supply is piped to rooms from the basement of the hospital. Water in a hydrating bottle on the wall is replaced with 45 to 90% alcohol, and oxygen is bubbled through this to the patient by means of a nasal catheter or BLB mask. No tent is used. Patient and visitors are cautioned not to smoke. Suction aspiration of pharyngeal mucus is occasionally used. The engineering department of the hospital objects strongly to this procedure. If a hazard exists, what precautions should be taken when the above mixture is given in a patient's room?*

R. P. Howard, M.D., Pocatello, Idaho.

Answer.—Alcohol in the pure state (200 proof) in air will flash in an open cup at about 80 F and in a closed cup at 60 F. If the alcohol is diluted to 90% or less it will require a higher ambient temperature to ignite it, but with pure oxygen instead of air the mixture will have a correspondingly lower ignition point. Because of these low ignition temperatures it would be possible for static electricity to provide a source of ignition. The resulting explosion and fire would shatter the bottle and cause the danger of flying glass moving at high speed. The alcohol-oxygen mixture so released could easily set flammable materials in a patient's room on fire. The procedure is highly dangerous and should be used as a method of therapy only with recognition of the calculated risk. Vaporization of alcohol as described in the inquiry is used occasionally throughout the United States. No fires or explosions are known to have occurred during such administration. Though the hazards are about the same as in anesthetizing areas, it is impractical to recommend that the treatment be given only in anesthetizing areas that conform to pamphlet no. 56. In a patient's room, all the precautions advised with regard to oxygen therapy should be followed rigidly, and, in addition, personnel serving the patient should be properly clothed to avoid the production of static electricity. It is fair to recommend that suction equipment be explosion-proof, preferably by use of a water-activated suction or a central suction system with the motors and pumps at a distant point. If a 30% alcohol solution in water is used with nebulization, there is no ignition hazard related to the alcohol; however, due to the high concentration of oxygen used, precautions, such as no smoking, must still be in effect. A 30% instead of a 45 to 90% mixture is recommended because it has been found to be as effective as higher concentrations of alcohol and because it reduces the fire hazard.

SWIMMER'S ITCH

To the Editor:—*It is known that schistosomiasis is prevalent in the waters from Puerto Rico to Japan and China, yet there seems to be a lot of doubt as to whether it is present in Korea. Last year the U. S. Army classified hundreds of different types of snails found in Korea and claimed that none of these were the hosts of the miracidia of schistosomes. In a recent issue of the* Annals of Internal Medicine *there was an article by a professor at the University of Puerto Rico who stated that in his experience, extending over a period of 12 years, he had examined many patients with schistosomiasis. He stated further that the cecariae of schistosomes could not live in salt water. However, the author of a recent article in* The Journal *claimed that schistosomiasis could cause swimmer's itch. The article did not state that this disease occurred as the result of swimming off the coast of Hawaii; however, it seems that other articles have cited this cause. If this is true, then the cecariae can live in salt water. An opinion on the subject would be appreciated, as there are many snails in Korea, particularly in the most desirable swimming areas. These are dotted with homes built by the Japanese who previously inhabited this area, and undoubtedly some of those persons had schistosomiasis japonicum.* *M.D., California.*

Answer.—Swimmer's itch is attributed to infestation of human skin with cecariae of avian schistosomes, which do not penetrate into the internal blood vessels. Originally these infestations were reported only from fresh water; however, recently some type of "swimmer's itch" has been reported from several coastal areas of North America and Hawaii. The details of schistosome species or of intermediate snail host species involved in these instances are not available. There are three species of the blood fluke Schistosoma which are parasites to man. S. mansoni is found in the West Indies and S. japonicum in the Far East. S. japonicum utilizes a single genus of snail (Oncomelania) as the intermediate host, while S. mansoni has a wider but still limited choice of snails for hosts. As the letter stated, apparently the right kind of fresh water snail is not found in Korea to serve as intermediate host for S. japonicum.

DISEASES FROM PERVIOUS TILE

To the Editor:—*Among the general requirements of the Plumbing Code in Miami, Fla., is the following regulation: "Plumbing fixtures shall be constructed from approved materials that have a smooth surface. They must be free from defects and concealed fouling surfaces and, except as permitted elsewhere in this code, shall conform in quality and design to one of the standard table no. 46-c. Fixtures constructed of tile and other pervious material and equipped with a waste outlet to retain water shall not be permitted." This is because of the grease and dirt that may be trapped between the tile and in the tile itself if it is not impervious; but if asked what diseases could be transmitted by the use of pervious tiles, with the exception of dermatophytosis, one would be at a loss. Are there other diseases so transmitted?*

William B. Welch, M.D., Miami, Fla.

Answer.—It is often difficult to cite the scientific basis for many provisions of sanitary codes. The provision in plumbing codes specifying that fixtures should have smooth, impervious surfaces that do not craze or crack is based on past experience that a porous or cracked piece cannot be cleaned in a bacteriological sense, even with great effort. It may be a source of great interest to some as to what types of organisms may find a suitable environment in these small cracks and pores and actually multiply. Several years ago, the U. S. Public Health Service, in collecting evidence for improving drinking fountain codes, cultured the organisms found on the walls of drain lines of existing drinking fountains. A wide variety of organisms, some pathogenic, were found, but to say that their presence contributed to disease transmission would be difficult to prove. Likewise, the presence of pathogenic bacteria lodged in the pore spaces of an unglazed plumbing piece cannot be proved to be the source of infectious disease, but it could be under certain circumstances. It should be borne in mind that bath tubs and even wash basins are reservoirs of dilute sewage in their intended function. Specifying only known cleanable surfaces as such may be easily justified on aesthetic grounds if not by the possibility of transfer of organisms from body openings from one person to the other.

AMPUTATION FOR GANGRENE

To the Editor:—*A 75-year-old woman, diabetic but not requiring insulin, has arteriosclerosis obliterans of lower extremities. She entered the hospital with beginning gangrene of the left foot. On physical examination, no arterial pulsations were felt below the femoral artery. Despite anticoagulant and antibiotic therapy and regulation of the diabetes, gangrene spread to involve the left lower extremity below the knee. Please comment on the best site for amputation—supracondylar or middle of left femur.* *M.D., Florida.*

Answer.—The proper level of amputation in this case depends on the extent of the gangrene. Preservation of the knee joint is of great importance, if it is possible. Amputation below the knee has the advantages of lower mortality, better chance for rehabilitation, and less tendency to stump pain. If gangrene does not extend up to the ankle, if the leg is warm, and if there is no contracture of the knee joint, a mid-leg amputation should be tried. If the gangrene extends to the ankle or above, a mid-thigh amputation is necessary. There are three types of thigh amputations. The Gritti-Stokes amputation is a supracondylar amputation which utilizes half of the patella for a weight-bearing stump. The Callander operation (*J. A. M. A.* 110:113-118 [Jan. 8] 1938) is a supracondylar amputation which removes the patella but uses the bed of this bone for a weight-bearing stump. Both of these operations are more likely to have postoperative complications than a mid-thigh amputation. At the present time most prostheses are fashioned for a non-weight-bearing stump and are very satisfactory. The operation which is least likely to cause complications and which produces a good end-result is a mid-thigh amputation.

RADIATION PROTECTION

To the Editor:—*Is there any possible danger to an x-ray technician under the following conditions? A 30-ma. diagnostic tube is used, with no fluoroscopy, at maximums of 85 kv. and 3 seconds with no more than 20 exposures per week, and a lead apron is worn.*

Leonard Casser, M.D., Cresskill, N. J.

Answer.—The radiation protection problem posed here involves a modest maximum workload of 20 exposures per week, partial protection of the technician with a lead apron, and a relatively low-capacity x-ray machine. Unfortunately, this is not sufficient information to determine whether the technician's radiation exposure exceeds the maximum permissible levels as specified by the National Committee on Radiation Protection. These recommendations, as stated in Handbook no. 60 (for sale by the Superintendent of Documents, Washington 25, D. C., at 20 cents), allow an average dosage of about 5 r to the whole or major part of the body per year. Under the worst combination of machine conditions and the technician's own work habits and techniques, the yearly maximum permissible dose could be exceeded within a few weeks. Under proper conditions, the technician should not receive more than about one-fourth or less of this exposure from the stated amount of work in a year. To estimate the exposure received, one needs to know the measured radiation output of the x-ray machine, whether the added filter and beam limitation by cone or diaphragm are adequate, and where the technician stands in relation to the x-ray tube and its primary beam and how far away during exposures. A properly shielded control booth should be used, and, of prime importance, the technician should never hold the patient or otherwise put a part of her own body in direct beam. The best way to find out if radiation protection is adequate is to have a protection survey performed by a qualified expert, usually a radiologic physicist. For regular work of this extent, it is advisable to monitor exposure with film badges, as are now supplied by a variety of commercial sources. By these means the safety of the technician can be assured.

DEATH FOLLOWING LYE BURN

To the Editor:—*A 50-year-old plumber knelt in lye, while working, and got extensive burns of both knees. He was treated with antibiotic ointments and two courses of tetracycline therapy, each of five days' duration. One month after the accident the patient became jaundiced; he showed congestive heart failure two days later and died after another three days. The pathologist reported fatty changes in the liver, kidneys, and heart; hypertrophy of the myocardium; coronary and aortic atherosclerosis; congestion and edema of the lungs; acute gastritis; edema of the brain; and ulceration of both knees. The patient drank heavily until a few years ago. Is there a possibility of a causal relationship between the accidental chemical burns and/or the treatment of them and his death? The patient is survived by his widow and nine minor children, and, since this is a compensation case, even the possibility of an aggravation of a preexisting condition by accident or treatment would help his nearly destitute family.*

Harry K. Grottewit, M.D., New York.

Answer.—Lye burns are strikingly restricted to the exposed area. No alkalies, as such, are absorbed, although profound shock may supervene. The interval of one month between the accident and the appearance of significant systemic involvement tends to minimize any primary connection between the accident and the subsequent death. While many antibiotics have caused disturbances chiefly on an idiosyncratic basis, the agents mentioned are not known to be outstanding in this respect. The autopsy report appears to indicate a series of long-standing degenerative processes. It is unlikely that the lye burns directly contributed to the death.

CORTICOIDS AND THE ASTHMATIC PATIENT

To the Editor:—*An asthmatic patient, during the postmenopausal period, has been treated with corticoids by other physicians. Under present treatment, her asthma has been improved sufficiently so that the dosage of hydrocortisone could be reduced to 7.5 mg. per day. However, she now shows evidence of classic moon face and fluctuating hypertension. Her 17-ketosteroid excretion per 24 hours is extremely low, indicating that under sudden stress she may die unless promptly and adequately sustained with steroids. She has a 4+ reaction locally when given an intramuscular injection of corticotropin gel and/or corticotropin-zinc hydroxide, with reactive areas of spongiosis 6 in. in diameter when either of these two products is injected. How should this patient be treated?*

Clifford H. Kalb, M.D., Milwaukee.

Answer.—Hydrocortisone might be given in gradually decreasing doses until the patient could be without it entirely for a while. ACTH could be given with an antihistamine, such as diphenhydramine hydrochloride, injected at the same time. If it is necessary to resume steroid medication, she should be given some other preparation, such as triamcinolone (9α-fluoro-16α-hydroxyprednisolone) or methylprednisolone. These newer preparations have less tendency to produce moon face and hypertension.

PAYMENT FOR OBSTETRIC CARE

To the Editor:—*What is the best manner for an obstetrician to go about billing his patients for prenatal care? If $75 of a $150 delivery charge is for prenatal care and $75 for the actual delivery, how should monthly bills be sent so as not to confuse the patient?* M.D., Texas.

Answer.—The method of handling obstetric fees varies with the doctor, the patient, and the locality. In any case the patient should be informed at the first visit what the fee will be and how it is expected to be paid. One big problem in charging for each prenatal visit is that many patients neglect their appointments, so that the physician could not divide the fee into two parts and still charge for each visit. A common method is to set the fee and ask the patient to pay half prior to delivery and the balance after delivery. Another method, which means extra bookkeeping, is to have the patient make a deposit at each prenatal visit. If seen early in her pregnancy she will have paid most of her bill before delivery. Most patients will carry out any method the physician decides on provided they are well informed about the system.

Answer.—The adjustment of obstetric fees varies from community to community and from doctor to doctor. Whatever plan is devised, no problems need arise if the patient and her husband have a full understanding of the fee program at the time of engagement of services. Most patients welcome a talk from the doctor along these lines but hesitate to introduce the subject. The doctor should take the initiative. In the case here presented, it would appear that $100 for delivery and hospital visits plus prenatal and postnatal office visits at a specific rate would simplify the situation. Extraordinary services at any period would be extra and should be so understood. It is easy enough to say at the conclusion of the first visit, "I suppose you and your husband would like to know something about the cost of all this." These are days of budgeted incomes, and let us hope that the role of the doctor as advisor and friend has not been lost in so-called medical progress.

OBESITY AND HYPOGONADISM

To the Editor:—*A 14-year-old boy weighs 155 lb. (70.3 kg.) and is 5 ft. 1 in. (154.94 cm.) tall. He has excessive fat around hips, abdomen, and breasts. He has a small penis and no male distribution of hair. His basal metabolic rate is –19%. Such measures to control weight as diet, thyroid administration, and therapy with dextro amphetamine sulfate have failed. Please describe further diagnostic measures and treatment.*

M.D., Oklahoma.

Answer.—The clinical description suggests that the patient may have a disorder of the hypothalamus with obesity and hypogonadism, resembling that originally described by Babinski and Frölich. This can be on the basis of a craniopharyngioma or other organic lesion, but more likely no gross intracranial pathology will be found. X-rays of the skull and for bone age should be obtained and the visual fields, urinary 17-ketosteroids level, and, if possible, levels of 11-oxysteroids, urinary gonadotropins, and serum protein-bound iodine (or radioactive iodine uptake) and urine concentrating ability determined. It is probable that the urinary 17-ketosteroids and gonadotropin levels will be low in this patient irrespective of whether a gross cerebral lesion is present. The thyroid function and urine concentrating ability should be normal unless a gross anatomic disorder exists. Treatment might consist of chorionic gonadotropin injections at a high dosage, 2,000 units three times weekly, for one to three months, or, alternatively, methyltestosterone, 5 mg. twice daily as a buccal tablet, with caloric restriction. This program would, of course, have to be extended if an organic lesion were present with or without other evidences of endocrinopathy.

FORMALDEHYDE HAZARD

To the Editor:—*Is there any information available regarding formaldehyde found in the blood stream of employees working in mills, plants, or stores selling or manufacturing the new resinate wash-and-wear garments? An article published in the* Daily News Record *regarding this subject reported on a plant closing in Phoenix, Ariz., recently because of illness resulting from employees handling urea formaldehyde resins. The Department of Health and Hospitals of Denver, Colo., has also sent out warnings regarding this problem.*

J. G. Probstein, M.D., St. Louis, Mo.

Answer.—The urea formaldehyde resins have long been in industrial use with many applications, such as a thermosetting glue in laminated wood production. Contact dermatitis may appear after exposure to the unpolymerized resins, but these substances chiefly are harmful because of allergenic properties, with the formaldehyde believed to be the more active fraction. Bronchial asthma may also be caused by these resins on an allergic basis. In the garments referred to in the query, the assumption is that polymerization is complete. Therefore, little difficulty should be expected from their wear, although, as a rarity, sensitization to the finished product might arise. There is no reason to believe that formaldehyde would appear in the blood stream of workers as a result of this exposure. This query is concerned only with stores selling these garments and factories manufacturing them. Here the exposure, if any, is minimal. In the manufacture of the resins themselves, the response might be different, since formaldehyde is a gas of well-established toxic properties.

SAFE MILK ABROAD

To the Editor:—*A diabetic patient is planning to travel in France and is worried about the directive issued by the U. S. Army that milk should be heated before it is safe to use. Is this true of the large cities, as well as of the rural areas? What advice should the patient be given?*

Joseph T. Beardwood Jr., M.D., Philadelphia.

Answer.—Nearly everyone in Europe boils milk before drinking it. This is done to kill any contaminating organisms and to retard souring. Even in countries where pasteurization is practiced, people continue to boil milk. As recently as 1955, the French Academy of Medicine passed a resolution requiring that all milk be boiled before use. This applied to both pasteurized and raw milk. Many animal diseases transmissible to man are spread by milk. Among the most common of these in Europe are bovine tuberculosis, brucellosis, and streptococcic infections. Milk may also be contaminated with any of the enteric types of bacteria. In some parts of Europe these diseases have been brought under control, e. g., Norway, Sweden, Denmark, and Holland. Other countries are making progress in eliminating these diseases, especially Great Britain, Germany, Switzerland, and Austria. The U. S. Army Veterinary Corps officers have the latest information on the best supplies of milk in Europe. They have done an excellent job of assisting milk producers and suppliers in providing a high quality product, but, lacking detailed knowledge and with wide variations still existing, a traveler would be well advised to drink only boiled milk.

STIPPLING OF ERYTHROCYTES

To the Editor:—*An employee in a paint factory is exposed to the fumes of benzene ring solvents. Two blood smears taken six months apart revealed stippling of his red blood cells. Otherwise he is apparently healthy. A dozen other employees in the factory who have a greater exposure to the benzene ring compounds do not show any stippling. Could this stippling be due to causes other than occupation? This employee does not handle lead.* *M.D., Illinois.*

Answer.—The query fails to note the exact benzene compounds to which exposure exists. The assumption is that toluene may be the chief component. Likewise, the query fails to provide information as to other hematological findings. An occasional stipple cell is a normal occurrence. If the exposure is to benzene itself, an increased number of stipple cells could appear, but a leukopenia is of greater significance. The actuality of benzene exposure may be indicated by the urine sulfate test. The ratio of inorganic sulfates to total urinary sulfates usually is at or above 85%. On exposure to benzene, this ratio may diminish to 70% or lower. Any ratio below 70% is significant. This test is not specific for benzene, nor is it a positive proof of benzene intoxication. Rather, it indicates some degree of exposure. Rarely, toluene modifies the blood findings, but this may be due to benzene as an impurity in the toluene. In the present instance, inquiry should be made as to lead exposure apart from work, but the qualitative demonstration of red blood cell stippling is in itself not diagnostic of lead poisoning.

OFFENSIVE SWEATING IN AN INFANT

To the Editor:—*A patient, 8½ months old, is apparently perfectly healthy, with no suggestion of rickets. He was never breast fed, but he seems to have developed normally. The mother says that frequently, for no apparent reason, and when even more lightly clad than the room temperature would dictate, he breaks out in a profuse sweat. In addition to this, the mother complains that when he sweats, and especially if this happens several hours after he has been bathed, he exudes an offensive body odor suggestive of an unbathed workingman. She is anxious to find some cause for both of these symptoms. A possible diagnosis of rickets does not seem to fit in with his history of adequate vitamin intake since birth.*

Frank Howard Richardson, M.D.
Black Mountain, N. C.

Answer.—An 8½-month-old infant with intermittent hyperhidrosis and bromhidrosis is rare. Bromhidrosis can be caused by such substances as garlic or sulfur-containing drugs, for instance, some of the newer drugs used to treat seborrhea. Arsenicals and bismuth can cause increased sweat and some odor. Those containing arsenic cause a garlicky or onion-like odor. The odor can be caused by the action of certain bacteria and/or fungi on the organic matter present in sweat areas. When the situation is intermittent, it is probably not advisable to use any drugs which are known to decrease sweat formation. More frequent bathing, with local application of a deodorant lotion or powder, may be helpful.

BICARBONATE TITRATION

To the Editor:—*Is the Haskins and Osgood modification of the Van Slyke and Cullen method for titrating the bicarbonate content of plasma as reliable in determining acidosis as the determination of the carbon dioxide combining power? What table or factor is used in connection with this procedure in deciding on therapy for acidosis or alkalosis?*

Donald F. Holm, M.D., Benson, Minn.

Answer.—Van Slyke, Stillman, and Cullen, in their original description of the procedure for titrating bicarbonate in plasma as compared to the earlier gasometric determination of carbon dioxide content, stated, "For clinical and most experimental purposes . . . it appears that the two methods give so nearly identical results that they may be used interchangeably." Haskins and Osgood modified the method because students had trouble in determining the end point of the titration. This still remains the chief objection to the method, but, with experience, results obtained by the titration method will be satisfactory. The gasometric method gives somewhat higher values. A factor to convert the value obtained by titrating the bicarbonate content of plasma to the carbon dioxide combining power is used as follows: Determine the number of milliliters of N/50 hydrochloric acid neutralized by subtracting the number of milliliters of N/50 sodium hydroxide used from the titration value of 5 ml. of acid. Multiply this figure by 22.4. The result will equal the alkali reserve or carbon dioxide combining power.

ENDEMIC GOITER

To the Editor:—*On visiting various villages during a two-week medical missionary itinerary into the jungles of British North Borneo, it was interesting to note that characteristic areas had certain problems. In particular, a 90% occurrence of colloid goiter of huge dimensions was encountered. The children of the village also had goiters, many of them with typical findings of cretinism. The youngest child with a large colloid goiter and cretin-like findings was 4 years old. Are any of these physical changes reversible by administration of thyroid to people of this area?*

Alfred O. Mazat, M.D., Singapore, Malaya.

Answer.—Endemic goiter occurs in several areas of the world and is considered the result of inadequate ingestion of iodine. Certain plants, for example, plants of the kale family, contain a goiter-producing substance. If plants containing such goitrogenic material are ingested in large amounts and at frequent intervals, goiter may result. One or the other or both of these causes probably accounts for the goiters described. It is most unlikely that these goiters represent familial goitrous cretinism, a rare condition. Desiccated thyroid administered to these individuals may be expected to correct hypometabolism and reduce the size of the goiters. It should not be expected to correct completely the mental and physical retardation which is a consequence of congenital hypothyroidism.

USE OF TOBACCO AND ALCOHOL AFTER CORONARY THROMBOSIS

To the Editor:—*A 53-year-old man is now apparently completely recovered, with normal electrocardiogram, from a coronary thrombosis. He has been doing his usual work for the past two months. Before the attack he took one drink of liquor and smoked three to four cigars daily. May he continue this routine now?*

Samuel S. Schept, M.D., Union City, N. J.

Answer.—Since tobacco is known to cause arterial vasoconstriction and since, occasionally, electrocardiographic changes of coronary insufficiency can be seen to occur in sensitive persons after smoking, the use of tobacco would seem contraindicated after coronary thrombosis. From a more practical standpoint, however, in the management of the entire patient it is at least equally important that he be emotionally rehabilitated, with the realization that his life can again be productive after a heart attack. If such rehabilitation requires that he be permitted to smoke a few cigars daily, it is probably more important that this be done than that the possible deleterious physiological effects be permitted to weigh too heavily. In general, moderation and not total abstinence would seem the most practical answer. Most persons who have had a complete functional recovery after coronary thrombosis may be permitted a drink of liquor and a few cigars daily if that was their lifelong habit previously.

DERMATITIS MEDICAMENTOSA

To the Editor:—*A patient developed a severe toxic dermatitis after a period of therapy with one of the new long-acting sulfonamides. Several months later, she still had a mottled erythematous discoloration of her face and arms, the parts most involved at the height of the dermatitis. The urine remained clear throughout the illness. How can this skin condition be cleared? What is the prognosis in regard to future systemic reactions to chemotherapy?* *M.D., Illinois.*

Answer.—Erythema after a severe drug dermatitis may persist for many months and probably represents a local vascular disturbance. Internal use of corticosteroids probably would cause prompt improvement but cannot be recommended for such a harmless condition. Topical creams containing hydrocortisone or prednisolone may be tried, and antihistamines may be given internally. This dermatitis apparently is an allergic response to the long-acting sulfonamide. The patient may have become sensitized also to other sulfonamides. Since she suffered from a severe dermatitis, it is likely that she would get another attack of the dermatitis if she received the same sulfonamide and would run a great risk in case some other sulfur preparation was given. This patient should avoid all sulfonamides in the future.

CHLORINATION OF WATER

To the Editor:—*In using a chlorine solution to make water safe for drinking, would a solution containing double the recommended amount of chlorine disinfect the water twice as fast?*

M.D., Indiana.

Answer.—In many situations the use of twice the chlorine dosage will halve the contact time required for disinfecting water. This is only an approximation, however, and is not universally true. The reactions of chlorine with various impurities in the water are complex, and the bactericidal effectiveness of chlorine depends on a number of factors, including temperature, type of chlorine residual (whether free or combined), hydrogen ion concentration, chlorine residual concentration, and the contact time. In all cases, it is the residual concentration after reaction with impurities rather than the chlorine dose that is significant in killing micro-organisms. Although the residual concentration will generally increase with increasing chlorine doses, there are situations where increasing the chlorine dose will actually result in a smaller chlorine residual.

BACTERIA COUNT OF YOGURT

To the Editor:—*What is the bacteria count of yogurt?* *M.D., Illinois.*

Answer.—Because yogurt is made in many ways, a precise estimate of the bacteria count is not possible except for individual batches or for the commercially prepared product which has been made under standardized conditions. The fermentation of milk to produce yogurt is controlled chiefly by temperature, by the use of special composite cultures, and by the use of milk which has been previously subjected to high heat treatment to destroy unwanted micro-organisms. Time is another factor. When the milk is first inoculated the bacteria count is low but increases rapidly to a peak, after which it tends to recede with changes in the pH of the product which is associated with the fermentation process. Thus, in commercially prepared yogurt the count tends to reach a high point, in the neighborhood of 500 million per cubic centimeter. This is followed by a diminution of the count to about 200 million.

SORBITAN METABOLISM

To the Editor:—*In what form, if any, would a sorbitan trioleate be metabolized by the human body? This and similar substances are used as emulsifying agents for some of the linoleic acid preparations now being marketed for the treatment of coronary artery disease. According to Kinsell, oleic acid, though unsaturated, is not sufficiently unsaturated to produce a significant hypercholesteremic effect. It may even neutralize the effect of linoleic acid. After these sorbitan trioleates are absorbed, metabolized, and utilized by the body as fats, is it not possible that they would antagonize the action of the linoleic acid relative to the effect on the blood cholesterol level?* *M.D., New York.*

Answer.—There is no cause for concern, because the amount of the emulsifying agent used is small and because oleic acid appears to be, so to speak, in a neutral corner. As compared to dietary carbohydrate, it neither raises nor lowers plasma cholesterol level in most of the patients studied thus far. It is probable that if one were to include a very high proportion of oleic acid with linoleic acid the net effect of the linoleic acid would be greatly diluted. Small amounts of oleic acid, whether as a glyceride or in other forms, will probably have a negligible effect on the lowering of the cholesterol level which one would expect from an adequate amount of linoleic acid preparation.

IMPOTENCE

To the Editor:—*At about what age, if any, may a presumption of impotence be fairly attributed to age? Is there any presumptive evidence of impotence in the objective appearance of an elderly man's genitals, such as pronounced and persistent relaxation or retraction, or in the status of the bulbocavernosus reflex? Is the frequency or infrequency of erotic dreams, with or without emission, any index of potency? Can any ingested substances, such as foods, drinks, additives, or drugs, cause a discoloration of semen that would be evident in an ejaculate?*

Joseph H. Toomey, M.D., New York.

Answer.—The male does not experience an abrupt cessation of sex hormone secretion. Potency may therefore continue undiminished for an indefinite period. Once the sex habit is well established, potency may persist even after castration. There is no age at which the human male can be presumed to be impotent. Objectively, there is no sign which is indicative of impotence. Marked relaxation and shriveling of the genitalia may suggest a cessation of sexual activity but are not absolutely diagnostic. Erotic dreams and nocturnal emissions are not at all uncommon in young or middle-aged men who are impotent, and these are no indication of a man's sexual potential. The color of the semen depends on flavins which are present in the seminal vesicular secretions. There is no known reference in the literature to discoloration following the ingestion of foods or drugs.

PRURITUS VULVAE

To the Editor:—*A 50-year-old married woman with definite menopausal symptoms who had a hysterectomy in 1953, including unilateral oophorectomy, has for the past six months had an itching, mildly vesicular eruption around the hairline surrounding the labia majora. There does not seem to be any intravaginal trouble. Mild lotions, sulfonamide ointments, and steroid preparations give only temporary relief. How can this annoying condition be cured?* *M.D., Mississippi.*

Answer.—One would think first of recurrent herpes simplex, the most feasible treatment for which would be the application of an ointment or lotion containing bacitracin. Repeated injections of smallpox or poliomyelitis vaccine are sometimes recommended, but too often the results are disappointing. Contact dermatitis from some irritant, such as nail polish, must be considered, but if this were the cause the irritation would not be confined to the one area. A fixed drug eruption is another diagnostic possibility. Such diseases as pemphigus or dermatitis herpetiformis are not likely to remain localized for a period of six months. Regardless of the cause, cool wet packs of a 0.5% solution of aluminum subacetate should afford relief from the itching.

CHRONIC AND RECURRENT FURUNCLES

To the Editor:—*A 12-month-old girl has had repeated crops of staphylococcic furuncles. Staphylococci of the same strain were found in the mother's nose. There has been response to no antibiotic except chloramphenicol, which has been used several times; obviously, repeated use is not advisable. Are there any indications and/or contraindications to the use of autogenous or stock vaccine?* *M.D., Pennsylvania.*

Answer.—There are no contraindications to the use of vaccine for the treatment of chronic and recurrent furuncles. The course of treatment, however, is necessarily prolonged, and the injections are painful. This treatment has been discarded by most physicians since antibiotic drugs became available, because the latter are much more effective. Usually treatment consists of cleansing the skin with a soap substitute containing hexachlorophene, adequate doses of an antibiotic agent to which the patient is not allergic and to which the infecting organism is susceptible, and the application of an ointment containing a combination of neomycin, bacitracin, and polymyxin B. If this regimen should prove inadequate, a search should be made for a systemic abnormality.

COLLECTION OF SEMEN SPECIMEN

To the Editor:—*What methods of collection of semen specimens for sperm counts in the diagnostic study of sterility are approved by the Catholic church?*

A. F. Merlino, M.D., Bedford, Mass.

Answer.—The methods which are acceptable to the Catholic church are as follows: (1) intercourse with a perforated condom, which allows some semen to be deposited in the vagina; (2) removal of semen immediately or soon after normal coitus from the genital tract of the woman; (3) direct removal of semen by aspiration from testes or epididymides; (4) expression of fluid by massage from seminal vesicles; (5) semen obtained as the result of spontaneous or involuntary emission; (6) extraction of seminal remnants about an hour after intercourse; (7) expression of male urethra after normal intercourse; and (8) collection of sperms (which would otherwise be lost) in a vaginal cup inserted in the vagina after intercourse.

VITAMIN K AND PERTUSSIS

To the Editor:—*A German article reports on the value of vitamin K in treatment of pertussis. If the reports are true, why is not vitamin K more widely known and used in this disease? The clinical picture of the baby sick with pertussis is indeed pitiful. Please give more information about why vitamin K is effective.*

R. P. Little, M.D., Schwelz, Switzerland.

Answer.—No control series on Vitamin K in pertussis therapy has followed the first report from Portugal and Spain, but a number of disappointing failures were reported from physicians in France, England, and the United States. It is not clear whether the reported successes are not perhaps analogous to such nonspecific old-style remedies as the exposure to gas, popular many years ago in the United States, or the ascent in an airplane to high altitudes occasionally employed in France. For the present this subject must remain open because of complete failure to confirm the findings by several interested individuals.

LINOLEIC ACID CONTENT OF NUTS

To the Editor:—*A great deal has been written lately about the role of linolenic acid in helping the body better to utilize the saturated fats. Please give a list of the common edible nuts with their respective content of linolenic acid. How much of these nuts one would have to eat to obtain a beneficial effect?* *M.D., New York.*

Answer.—Figures for linolenic acid content of nuts are not available. The following figures, taken from an article by Hayes and Rose (*J. Am. Dietet. A.* 33:26, 1957), represent the amount of linoleic acid present in some common edible nuts: almonds, 12 to 15 nuts or 15 Gm., 1.54 Gm. of linoleic acid; peanuts (roasted), 15 to 17 nuts or 15 Gm., 1.72 Gm.; pistachio nuts, 30 nuts or 15 Gm., 1.56 Gm.; and English walnuts, 8 to 15 halves or 15 Gm., 6.20 Gm. It is impossible at present to suggest any particular quantity of these nuts as being desirable to ingest daily.

PROGRESSIVE PIGMENTARY DERMATOSIS

To the Editor:—*What is the cause, pathogenesis, and treatment of progressive pigmentary dermatosis?*

Mervin Rosenberg, M.D., Northwood, N. D.

Answer.—Progressive pigmentary dermatosis is a subacute inflammatory skin disease affecting chiefly the lower extremities. It is characterized by groups of red, yellow, or brown puncta that develop into patches. There is a gradual extension of the process over the legs, feet, and thighs. The upper extremities and trunk, too, may be involved, although less often. The older lesions turn brown and then gradually fade. The process is apparently not due to impaired circulation. The red components differ from the darker hues found in stasis dermatitis. This disease clears spontaneously after months or years. There are no subjective symptoms. The cause is unknown, but hypercholesteremia has been found in a number of cases. No treatment is effective nor is any necessary, because almost always the only affected parts are covered by clothing.

VETERINARY ANTIBIOTICS

To the Editor:—*Is there any essential difference in the antibiotic drugs used for human beings and domestic animals? A patient who used veterinary penicillin on himself got a severe allergic reaction, whereas no reaction occurred with that made for human use.*

James W. Miller, M.D., Greensburg, Ky.

Answer.—Under section 507 of the Food, Drug, and Cosmetic Act, the standards of identity, strength, quality, and purity for veterinary and human penicillin are the same. With few exceptions, the standards are the same also for veterinary and human streptomycin, dihydrostreptomycin, chlortetracycline, tetracycline, bacitracin, and chloramphenicol. If an allergic reaction is obtained with a bottle of penicillin labeled as veterinary and later the same patient failed to react with a bottle of penicillin labeled for human use, the reaction is not related to the drug but to the allergic state of the patient.

DIVERTICULITIS

To the Editor:—*What is the dosage of and manner of prescribing barium sulfate in the treatment of diverticulitis?* *M.D., New Jersey.*

Answer.—Barium sulfate, either taken by mouth or given by enema, was formerly used as a treatment of diverticulitis. Today it is generally not considered good treatment.

NARCOTICS AND GLYCOSURIA

To the Editor:—*Can the use of narcotics (including marihuana) cause sugar in the urine without the presence of clinical diabetes? Can it elevate the blood cholesterol level? Would such persons show evidence of liver damage as demonstrated by laboratory tests?* *M.D., Illinois.*

Answer.—There is no evidence that the chronic use of narcotics (opiates and synthetic analgesics) or marihuana can cause sugar in the urine or induce liver damage. No reports have been noted on the effect of narcotics on the blood cholesterol level. These drugs induce moderate hyperglycemia in sufficient dosage. Patients addicted to narcotics frequently eat an inadequate and unbalanced diet with a preponderance of "sweets"; consequently, pathology is often observed which is related primarily to the defective diet rather than to the use of narcotics per se.

COOKING FATTY ACIDS

To the Editor:—*To what extent does heat used in cooking (pan frying, baking, pressure cooking, and deep fat frying) alter the degree of unsaturation of fatty acids present in the commonly used cooking oils?*

James L. Turner, M.D., Oakland, Calif.

Answer.—According to Deuel (Lipids, New York, Interscience Publishers, Inc., 1957), the temperature at which polymerization occurs is at a higher level than that to which food fats ordinarily are subjected. Generally, polymerization will only occur when these high temperatures are maintained for periods of 8 to 12 hours. Therefore, there is apparently little possibility of the unsaturated fatty acids being polymerized under ordinary cooking conditions.

HEMOGLOBIN LEVEL IN CHILDREN

To the Editor:—*To estimate the hemoglobin level in children, a colorimetric method is being used by some workers. A finger of the child is inserted into such an apparatus, and, without the skin being pierced, the hemoglobin level is estimated by transillumination. Can even remote accuracy be achieved with such a method?*

H. H. Neumann, M.D., Elmont, N. Y.

Answer.—Such a method is employed to measure oxygen saturation of the blood, but it could not give an accurate measurement of hemoglobin concentration.

COMSTOCK SYRINGE

To the Editor:—*It is deduced from a quotation in Himes' "Medical History of Contraception" (Baltimore, William Wood & Company, 1936) that the Comstock syringe is some sort of vaginal douche apparatus. How does it work?*

M.D., Massachusetts.

Answer.—The Comstock syringe is used for cleansing the vagina for purposes of contraception. It consists of a tubular speculum made of either rubber or glass. At one end is a large rubber bulb. The bulb is filled with fluid and the instrument inserted into the vagina; the fluid is then expressed by pressure of the bulb and withdrawn back into the syringe when the bulb is released. This cleanses the vagina thoroughly.

Reference

Herrick, O. E.: Abortion and Its Lesson, Michigan M. News **5**:710, 1882

ILEAL RESERVOIR (URETEROILEOURETHRAL ANASTOMOSIS)

METHOD OF URINARY DIVERSION

George T. Mellinger, M.D.
and
Garfield L. Suder, M.D., Cincinnati

Ureteroileourethral anastmosis is a new method of urinary diversion which allows a patient to void in the normal manner. This is a procedure which permits complete removal of the bladder without likelihood of retrograde kidney infection. The left ureter is transplanted to the side of the isolated ileal segment near its proximal end, and the right ureter is anastomosed to the side of the loop distal to the left ureter. The loop is doubled back on itself, and the urethra is joined to the side of the loop just proximal to the distal end. A catheter is passed through the urethra into the new bladder and remains in place for three weeks. There does not appear to be any disturbance of electrolyte balance through absorption from the segment.

Recently, due to growing recognition of the value of radical surgery of the bladder, there has been increased interest in techniques of urinary diversion. This interest was highlighted by the development of the ileal conduit operation, which supplanted ureterosigmoidostomy with its occasional sequelae of ascending renal infections, hydronephrosis, and hyperchloremic acidosis. Merrick's ileocecal bladder eliminated the principal objection to the conduit procedure—that is, the necessity of wearing cumbersome urinary appliances—but it required insertion of a catheter through the abdominal ileostomy opening to evacuate the bladder.

A procedure which permits complete removal of the bladder without likelihood of retrograde kidney infection and which enables the patient to void in a normal manner should be welcomed. In 1951, in Paris, Couvelaire[1] anastomosed the side of the lower end of an isolated loop of ileum, to which the ureters had been joined, to the prostatic urethra. The upper end of the loop was brought to the surface of the abdomen as in an ileostomy. Later, the ileostomy was closed and the patient was able to void. In Leeds, Pyrah[2] used a somewhat similar technique in two patients, and his colleague, Mr. Raper, operated on a third patient in like fashion. Makuuchi[3] carried out the procedure in five patients, using the sigmoid instead of ileum in one.

Pyrah's technique consists of anastomosing the ureters into the two ends of an isolated ileal loop. Then the urethra is joined to the side of the midportion of the isolated segment. In all instances, the patients voided easily and had good continence. There was complete absence of ureteric reflux in all cases and only a small amount of residual urine. Intravenous urograms three months postoperatively showed no dilatation of the upper urinary tract.

In this procedure the drainage from the left ureter easily passes down the ileum in an isoperistaltic direction on its way to the urethra. However, as urine must pass in an antiperistaltic direction on the right side, increased pressure within the right upper urinary tract may occur in later years. To circumvent this possible complication, we decided to modify the technique as follows: The left ureter is transplanted to the side of the isolated ileal segment near its proximal end, and the right ureter is anastomosed to the side of the loop distal to the left ureter. The loop is doubled back on itself, and the urethra is joined to the side of the loop just proximal to the distal end (fig. 1). A catheter is passed through the urethra into the new bladder and remains in place for three weeks.

Report of Cases

CASE 1.—A 26-year-old male was referred by his private physician with a diagnosis of carcinoma of the bladder. During the previous year, he had been confined to three different hospitals for persistent frequency, urgency, and marked dysuria with hematuria. Several cystoscopic examinations were performed during this period, all of which led to a diagnosis of cystitis. In December, 1957, transurethral biopsy of the bladder showed a transitional-cell carcinoma of the bladder, and on Jan. 21, 1958, he was admitted to the Veterans Administration Hospital, Cincinnati. He had lost about 13 lb. (6 kg.) during the 10 months before admission.

This well-developed but thin patient had a blood pressure of 120/75 mm. Hg. No costovertebral angle tenderness was elicited, and the liver, spleen, and kidneys were not palpable. There was some tenderness in the suprapubic area. The prostate was firm, and no masses were felt in the region of the bladder. Culture of the urine showed Pseudomonas aeruginosa. The blood urea nitrogen level was 12 mg. per 100 cc., sodium level 147.5 mEq. per liter, chloride level 107 mEq. per liter, potassium level 4.9 mEq. per liter, and carbon dioxide–com-

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From the Veterans Administration Hospital and the University of Cincinnati.

bining power 23.2 mEq. per liter. Intravenous urography was essentially normal, and osseous metastases were not seen radiographically.

On Feb. 12, 1958, with the patient under general anesthesia, and through a Cherny incision, a total cystectomy was performed, and at the same time approximately three-quarters of the prostate gland was removed. The peritoneum presenting through the wound was opened in the midline, and an appendectomy was performed. A segment of intestine approximately 10 in. long and 6 in. distal to the ileocecal valve was isolated, and the ends of the segment were closed, with use of an inner layer of catgut suture and an outer layer of silk. After the intestine had been anastomosed, the isolated segment was brought down through the peritoneal opening, and the peritoneum was closed about the mesentery. The left ureter was then anastomosed to the side of the proximal end of the segment, with use of a Nesbit mucosa-to-mucosa technique. In the same manner, the right ureter was anastomosed to the segment about 3 in. distally. The intestine was bent into a "C," and the prostatic capsule and urethra were sutured to an opening in the side of the segment approximately 2 in. proximal to the distal end. A 18 F. Foley catheter was passed through the penis into the ascending limb of the segment, and the bag was distended with 30 cc. of clear water. Drains were placed, and the wound was closed.

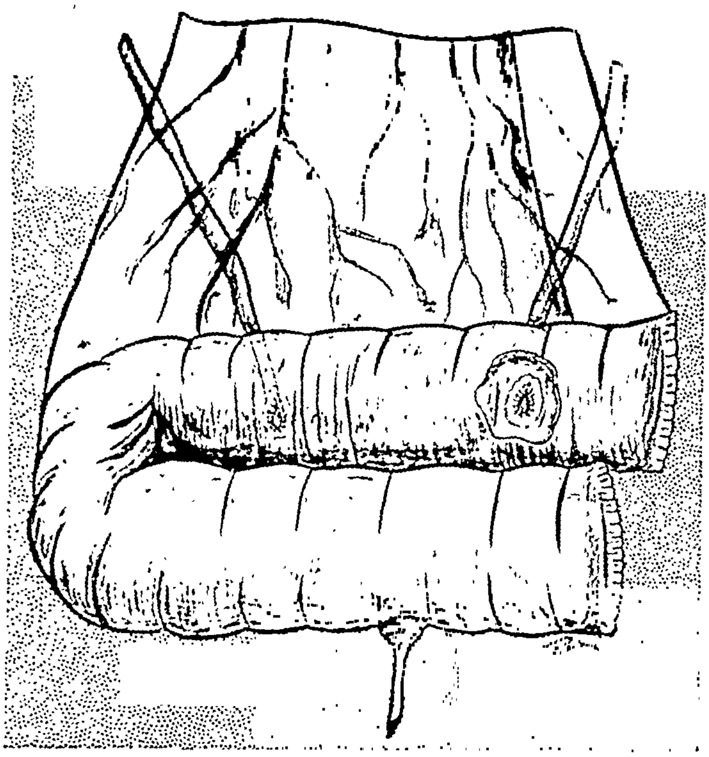

Fig. 1.—Ileal reservoir on completion of surgery.

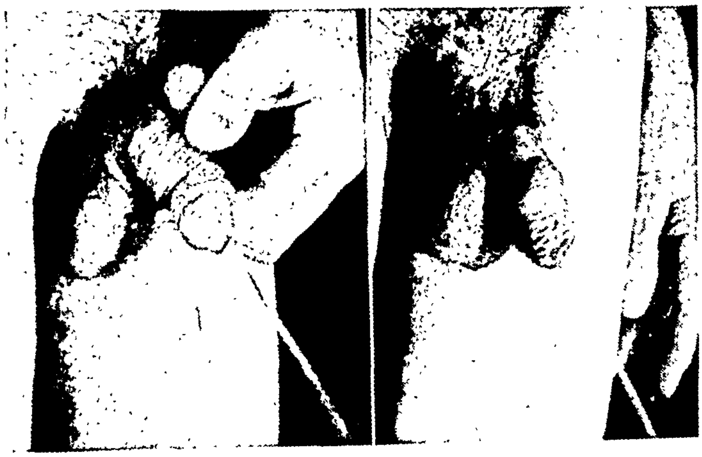

Fig. 2.—*Left* (case 1), patient voiding, with good stream, six weeks postoperatively. *Right* (case 2), patient voiding, with good stream, eight weeks postoperatively.

After removal of the urethral catheter three weeks postoperatively, the patient voided well and easily. He was continent during the day but had stress incontinence at night during the first two weeks. At first, micturition took place about once every hour. After two months, he urinated about every two and a half hours (fig. 2, *left*), passing 7 oz. of urine, with less than 20 cc. of residuum, and was completely continent.

Intravenous urography performed two months postoperatively showed normal results. On March 25, 1958, approximately six weeks postoperatively, the serum chloride level was 100 mEq. per liter, serum sodium level 150 mEq. per liter, and serum potassium level 4.8 mEq. per liter.

The patient returned to work. Four weeks later, toward the end of April, he began complaining of pain in the musculature of the back from the sacroiliac junction to the upper rhomboid area. There was considerable spasm of the sacrospinalis muscles but no costovertebral angle tenderness. Radiographic examination of the thoracic and lumbar vertebrae failed to demonstrate metastases.

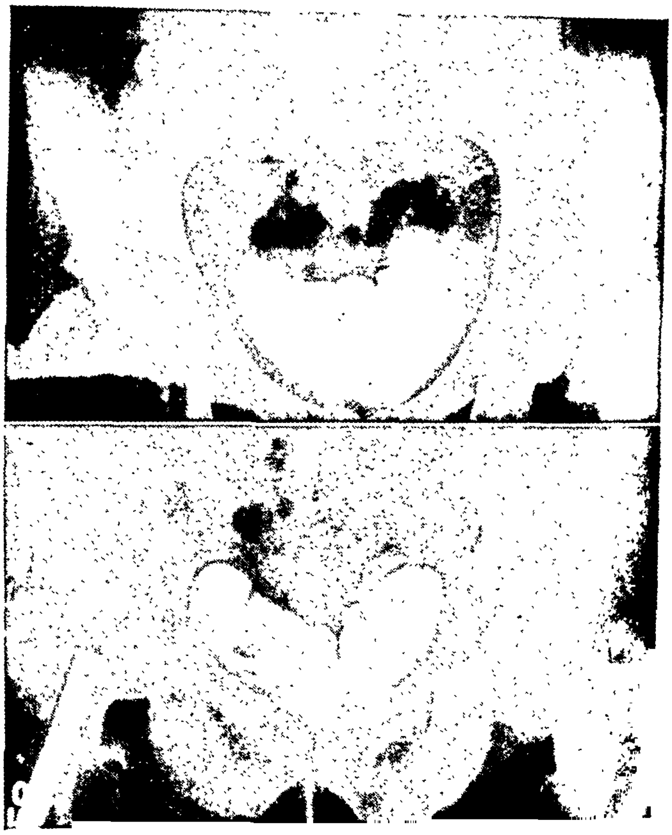

Fig. 3.—*Top* (case 1), cystogram taken four weeks postoperatively. Note absence of ureteric reflux. *Bottom* (case 2), cystogram taken eight weeks postoperatively, showing bilateral ureteric reflux.

After readmission of the patient on May 12, 1958, a spinal tap demonstrated partial subarachnoidal block. Shortly afterward the patient died. Autopsy showed several preaortic and iliac lymph nodes involved by metastases from the carcinoma of the bladder. The bodies of the thoracic and lumbar vertebrae were infiltrated with transitional cell carcinoma. The bladder substitute showed no inflammation. The ureteroileal junctions were open and without stricture, and the ureters were not dilated. The kidneys were the seat of chronic pyelonephritis. A large metastatic nodule was found in the liver. With hindsight, we feel that the lesion of the bladder had been present too long prior to treatment for a successful result.

Case 2.—A 69-year-old male was referred by his private physician to the Veterans Administration Hospital, Cincinnati, on March 15, 1958, because of painless gross hematuria of two weeks' duration. When first seen, he had complete retention of urine and was in great pain. The blood pressure was 175/80 mm. Hg, and the bladder was palpable above the pubis, but there was no costovertebral tenderness. We removed 740 cc. of grossly bloody urine from the bladder by catheter. The hemoglobin level was 6.6 Gm. per 100 cc. and hematocrit reading 21% before the patient received a transfusion of whole blood.

On March 20, 1958, a cystoscopic examination revealed multiple papillary carcinomas of the bladder. A biopsy specimen was taken from the lesions, and the histological report was papillary carcinoma. Culture of the urine showed Alcaligenes. The blood urea nitrogen level was 20 mg. per 100 cc., sodium level 144.5 mEq. per liter, chloride level 100 mEq. per liter, potassium level 3.8 mEq. per liter, and carbon dioxide–combining power 18 mEq. per liter. A normal pyelogram of the right side appeared on intravenous urography, and a nonfunctioning kidney was found on the left. Osseous metastases were not seen radiographically.

On April 14, 1958, a total cystectomy, prostatectomy, and ureteroileourethral anastomosis were performed, using a technique identical to that in case 1. The patient voided well and easily when the urethral catheter was removed. At night there was some stress incontinence, but he had complete control during the day. He now voids about every one and a half hours (fig. 2 *right*), passing 4 oz. of urine with less than 30 cc. of residuum.

Intravenous urography performed three weeks postoperatively showed a normal right pyelogram and prompt excretion of pyelographic material on the left, with mild caliectasis. On June 9, 1958, the blood urea nitrogen level was 20 mg. per 100 cc., sodium level 152.5 mEq. per liter, chloride level 104 mEq. per liter, potassium level 4.8 mEq. per liter, and carbon dioxide–combining power 20.7 mEq. per liter.

The patient is able to recognize when the bladder is distended and to void without exerting manual pressure on the abdomen. Postoperative cystogram shows reflux up both ureters, most marked on the left, which was the side that showed no function preoperatively.

Comment

Both patients were able to recognize when the bladder was distended and to void without exerting manual pressure on the abdomen. Both were continent during the day but had some difficulty maintaining continence during sleep.

As in cases previously reported by others, postoperative cystograms in our case 1 showed absence of ureteric reflux. However, the patient in case 2 has slight reflux up the right ureter and complete filling of the left ureter and renal pelvis.

These two patients were able to retain urine over two and one-half and one and one-half hours, respectively, without voiding. They evacuated at least 4 oz. and had residual amounts of urine of less than 30 cc. Studies of blood electrolytes have shown no variation since prior to surgery. The intravenous urograms were normal at the time of the death of the patient in case 1, and in case 2 the patient showed regained function in the left kidney postoperatively, while the right side remained normal.

The cystograms for both patients (fig. 3) showed good appearance of the ileal reservoir. The cystometrogram for the patient in case 2 (fig. 4) demonstrated a pattern of intestinal motility. When the bladder contained 70 cc. of water, the pressure spiked to 71 cm. H_2O, which should have been sufficient to allow voiding. During the procedure, maximum pressure reached 82 cm. without straining at a volume of 132 cc. At 250-cc. volume, the patient stated that he had attained his maximum capacity, at which time the pressure was 62 cm. H_2O. By straining, he succeeded in raising this pressure to 91 cm. We intend to perform cystometography at intervals on this patient to determine if the pattern remains intestinal or changes later to that more typical of a normal bladder.

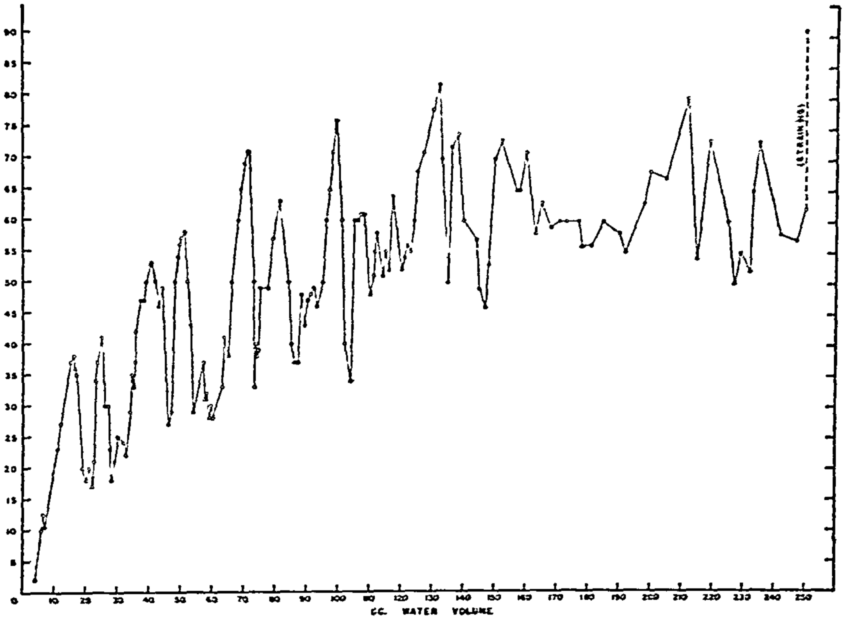

Fig. 4 (case 2).—Cystometrogram, six weeks postoperatively, demonstrating intestinal pattern.

Summary

Ureteroileourethral anastomosis is a new method of urinary diversion which allows a patient to void in the normal manner. We feel that after cystectomy for carcinoma of the bladder it may be preferable to other methods of diversion. There does not appear to be any disturbance of electrolyte balance through absorption from the segment. Cystometrographically, the new bladder shows an intestinal pattern. We have performed this operation in two patients and feel that it merits further study and consideration.

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CLINICAL NOTES

ACUTE RENAL FAILURE AFTER INTRAVENOUS PYELOGRAPHY IN PLASMA CELL MYELOMA

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In 1954, Bartels and his associates[1] reported a patient with plasma cell myeloma (multiple myeloma, myelomatosis) who developed acute renal failure immediately after intravenous pyelography. Three additional patients with plasma cell myeloma, in whom intravenous pyelograms appear to have precipitated oliguria or anuria, have been described in the Scandinavian literature.[2]

Recently, we have observed this phenomenon in a patient with plasma cell myeloma in whom normal renal function was demonstrated immediately prior to pyelographic examination. Our observations of this patient have indirectly led to the recognition of pyelography-induced anuria in a woman with plasma cell myeloma.[3] The purpose of this communication is to focus attention on the potential danger of intravenous pyelography in patients with this disease and to discuss the pathogenesis of the acute renal failure in these patients.

Report of a Case

A 34-year-old man was admitted to the medical service of the West Haven Veterans Administration Hospital on July 9, 1957, with complaints of bone pain, nausea, and vomiting. He had been transferred from another hospital, where he had been admitted on June 30, 1957, for evaluation of low back pain and proteinuria.

Results of a physical examination at that time, including a blood pressure of 134/80 mm. Hg, were entirely normal. Laboratory data showed a hemoglobin level of 9.6 Gm. % and a sedimentation rate of 28 mm. per hour (Wintrobe). The white blood cell and differential counts were within normal limits. Urine analyses were entirely normal except for proteinuria. The serologic test for syphilis was nonreactive. The blood urea nitrogen level was 11 mg. % and the creatinine level 1.3 mg. %. The total serum protein level was 10.2 Gm. %, with an albumin level of 2.6 and a globulin level of 7.6 Gm. %. Serum electrolyte and liver function determinations were normal except for a thymol turbidity of 15 units. Roentgenograms of the spine showed generalized demineralization, with multiple small osteolytic lesions of the vertebral bodies and ribs. Plasma cell myeloma was suspected.

On July 3, 1957, intravenous pyelograms with sodium acetrizoate (Urokon sodium) were performed. These showed normal excretion of the contrast medium and normal renal structure. This test had been preceded by the administration of a cathartic and of a saline enema. Nausea and vomiting developed on the day after pyelography, and parenterally given fluids were required to maintain hydration. Unfortunately, observations of urine output were not recorded during the next few days. The diagnosis of plasma cell myeloma was established thereafter on the basis of Bence Jones proteinuria and a bone marrow aspiration.

On the seventh day after pyelography the patient was transferred to this hospital. Physical examination revealed a blood pressure of 150/100 mm. Hg, a pulse rate of 120 beats per minute, a respiration rate of 20 per minute, and a temperature of 100 F (37.8 C). Except for conjunctival pallor, crusted blood in both external nares, and vertebral tenderness, the examination was negative.

The patient's blood urea nitrogen level on admission was 100 mg. % and the creatinine level 12.8 mg.%. Laboratory evaluation otherwise confirmed the findings recorded at the first hospital. In addition, the urine showed 4+ proteinuria, a specific gravity of 1.012, and a few red blood cells and white blood cells in the sediment. Phenolsulfonphthalein excretion was 15% in two hours. An abnormal gamma globulin peak was observed in the serum and a slow beta peak in the urine by electrophoresis. Blood studies were performed with great difficulty due to the presence in the blood of cryoglobulin.

The patient's course was one of progressive renal failure complicated by recurrent epistaxes, nausea, and vomiting. Urine output on the day after admission was 500 cc. but rose to more than a liter each day. Despite treatment with urethan, radiation, and adrenal steroids and transfusions the patient died in uremia almost three months after pyelography.

Autopsy showed large kidneys (350 Gm.), which appeared normal except for purplish discoloration of the cortex. Microscopically the glomeruli appeared normal. The tubules were, in general, markedly dilated and filled, particularly in the proximal portions, with deeply eosinophilic inspissated casts in varying stages of evolution. The tubular epithelium was intact in some areas and sloughed in others. There was no reaction to some casts, but others were invested by flattened

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cells or by multinucleated giant cells (see figure). Occasional cast material was deposited on a giant cell surrounding an earlier cast. The interstitial tissue was relatively free of cellular exudate. Several tubules contained rounded crystals which polarized light. The calyceal epithelium was intact, but the subcalyceal tissue was edematous and hemorrhagic. No vasculitis was present.

Comment

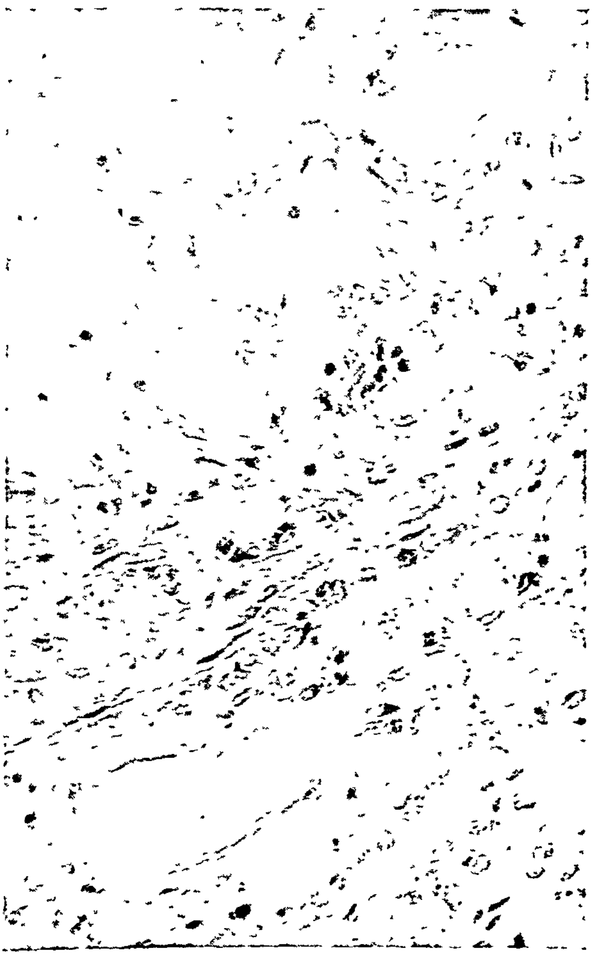
Fatal complications of intravenous pyelography are extremely rare. Pendergrass and co-workers[4] reported only 31 deaths in more than 3,800,000 intravenous pyelographic examinations. Twenty-five of these deaths occurred immediately after intravenous injection of the contrast substance and were preceded by evidences of anaphylactoid shock, cardiac arrest, or symptoms of drug sensitivity. Three of these patients died in uremia within a few days of the examination, but the clinical data in these three cases are too scant to permit careful evaluation.

None of the five patients with plasma cell myeloma in whom pyelography is reported to have precipitated acute renal failure exhibited any of the features of drug allergy to the three different iodinated contrast mediums employed. Neither convulsions nor shock occurred during or after the procedures. Anuria or oliguria was noted shortly after completion of the procedure, and clinical and laboratory confirmation of acute renal failure was quickly obtained. Three of these patients died in acute renal failure 8, 11, and 40 days after the onset of anuria. Although two of them survived the oliguric phase, death in uremia followed within a few months. Each of the authors firmly believed that the pyelography had precipitated the sudden renal decompensation.

Renal disease in plasma cell myeloma occurs in more than half of the patients.[5] Characteristically, chronic progressive uremia develops in the absence of hypertension, hematuria, edema, or retinal abnormalities, and occasionally the presenting complaints are the symptoms of far advanced renal decompensation. Kolff[6] has stated that patients with plasma cell myeloma who have "... slightly impaired renal function, for reasons unknown, suddenly may go into (recoverable) acute anuria." In our experience this phenomenon is quite unusual.

Much has been written about the pathogenesis of myelomatous renal disease, but few authors have disagreed with Bell's hypothesis.[7] He stated, in his excellent paper on this subject, that the process was essentially a mechanical one, with the deposition of Bence Jones protein casts causing blockage of the renal tubules and subsequent atrophy of the involved nephrons. Oliver[8] has supported this "stopped pipes" theory by his morphologic demonstrations. Forbus and his co-workers[9] emphasized the presence of foreign body giant cell reaction induced by the abnormal protein coagulum. Renal biopsies have recently shown that these microscopic changes, which are not always associated with Bence Jones proteinuria, may occur during life[10] and are not merely terminal changes as has been suggested.[11]

Clinical and laboratory aspects of the five cases of pyelography-induced anuria are summarized in the table. It is interesting to note that the diagnosis of plasma cell myeloma had not been established in any of these patients at the time pyelography was performed, although it was suspected in several. Renal function was significantly impaired in one patient but seemed normal or nearly so in the others on the basis of concentrating ability, blood urea nitrogen level, urea clearance, and normal pyelographic visualization. With one exception these patients were normotensive.



Dilated tubes, many of which are filled with eosinophilic homogeneous casts. Large multinucleated giant cell is in lower right.

Abnormal urinary proteins were present in the four cases in which it was sought. The electrophoretic patterns of the serum proteins varied, showing a normal pattern in one, an "M" peak in one, and a gamma peak in a third. Serum calcium determinations were normal in the two cases in which they were reported. Roentgenograms showed characteristic osteolytic lesions in four patients.

The pathological findings in these patients at autopsy showed little or no involvement of the glomeruli. There were varying degrees of homogeneous, eosinophilic, proteinaceous casts in the distal convoluted and collecting tubules. In one of these patients autopsy on the ninth day of oliguria revealed only a few such casts. Some dilatation of the tubules and atrophy of the tubular epithelium was present. There was moderate infiltration of the interstitial cells with lymphocytes, plasma cells, and macrophages. There was no evidence of vascular reactions or other types of renal disease.

How can the pathogenesis of such lesions be explained? Although simple dehydration with the intratubular precipitation of urinary protein is not an entirely satisfactory explanation, it appears to fit the clinical and pathological features of the syndrome more closely than any other apparent explanation.

Intravenous pyelography in a number of ways may set the stage for this intrarenal protein coagulation. Caster-oil cathartics and enemas are routinely used to permit optimal visualization of the renal structures. Dehydration produced in this manner may be compounded by the restriction of fluids designed to depress urine flow. Abdominal compression, which is used to increase the concentration of the excretory dye, has been shown by Bradley and Bradley [12] to reduce renal blood flow and to produce a scant concentrated urine. It is interesting to note that Addis [13] has reported the onset of anuria in a patient with plasma cell myeloma after the development of dehydration induced by castor oil. Similarly, Thaysen [14] has mentioned a patient with plasma cell myeloma in whom acute renal failure followed nausea and vomiting.

Clinical and Laboratory Aspects of Five Cases of Pyelography-Induced Anuria

Author	Age, Yr.	Sex	Complaint	Blood Urea Nitrogen Level, Mg./100 Ml.	Proteinuria, Gm./100 Ml.	Bence Jones Protein	Specific Gravity	Contrast Substance	Visualization	Outcome	Remarks
Bartels and others[1]...	69	M	Fatigue, full flank	81	1.0	...	...	Iodopyracet (Diodone)	Poor	Death	Death 40th day; autopsy: cast-plugged tubules
Myhre and others[2a]...	70	M	Back pain	30	1.8	+	1.029	Diodonediaethanolaminum (Nycotrast)	Good	Death	Death 11th day; no autopsy
Myhre and others[2a]...	42	M	Ulcer	36	1.2	+	1.032	Diodonediaethanolaminum	Good	Recovery	Died in uremia 8 mo. later; autopsy: cast-plugged tubules
Killmann and others[2b]	36	M	Back pain	...	10-15 per day	+*	1.027	Iodopyracet	Good	Death	Death 9th day; autopsy: few tubular casts
Perillie and Conn.....	34	M	Back pain	11	possible	+	1.026	Sodium acetrizoate	Good	Recovery	Death 3 mo. later; autopsy: cast-plugged tubules

* Abnormal protein.

It seems likely that saturation of tubular urine containing a large amount of an abnormal easily precipitable protein may satisfactorily explain the intratubular precipitation of this material. The sudden blockage of a large percentage of the renal tubules may result in sudden suppression of urine flow. Although the effect of the pyelographic contrast substance itself in vivo is unknown, it does not cause precipitation of Bence Jones proteinuria in vitro. The degree of acidity, the concentration of urinary electrolytes and urea, and other unknown factors are difficult to evaluate. Urinary acidity was not altered, however, after intravenous pyelography with sodium acetrizoate or diatrizoate (Hypaque) sodium.[15]

Even in plasma cell myeloma the precipitation of acute renal failure by intravenous pyelography is an unusual event. There were no reactions, either immediate or delayed, in the 11 myelomatous patients in whom intravenous pyelograms were performed at these hospitals.

The fact that acute renal failure occurred in each of these patients prior to the establishment of the diagnosis of plasma cell myeloma suggests that all patients with unexplained proteinuria should be evaluated for this disease prior to the performance of intravenous pyelography. Of perhaps greater clinical significance is the implication that acute renal failure in plasma cell myeloma may be precipitated by dehydration. It follows that less severe degrees of renal disease in this disease may be initiated or aggravated by dehydration. It would appear wise to assure maximal urinary output in all patients with this disease, particularly those with proteinuria, as a means of preventing or minimizing myelomatous renal disease.

Summary

Acute renal failure may develop immediately after intravenous pyelography in patients with plasma cell (multiple) myeloma. At autopsy these patients, in whom abnormal proteinuria had been demonstrated, showed plugging of the renal tubule by coagulated protein casts. We postulate that in the presence of Bence Jones proteinuria the dehydration produced by fasting and purging and the increased concentration of urine caused by abdominal compression may combine to cause precipitation of the urinary protein within the renal tubules. This internal obstructive uropathy may be prevented by avoiding intravenous pyelography in patients with plasma cell myeloma or proteinuria of undetermined cause. If acute renal failure is precipitated in these patients by simple dehydration, it is important to assure adequate fluid intake at all times.

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The authors wish to thank Dr. R. Yesner for his interpretation of the pathological material.

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SIMPLE METHOD FOR DETECTION OF PHENYLKETONURIA

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Phenylketonuria is a disease characterized by the inability to metabolize an essential amino acid, phenylalanine, which is present in all proteins in average concentration of 4%. Phenylalanine, phenylpyruvic acid, ortho-hydroxyphenylacetic acid, and other unusual metabolites are excreted in the urine. This biochemical abnormality ordinarily leads to severe mental defect. Excellent reviews[1] have appeared recently.

Results have been reported[2] indicating that treatment with diets low in phenylalanine has been successful in allowing normal physical and mental growth. It appears, therefore, increasingly important to detect phenylketonuria in early infancy. A routine diaper test[3] has been in use in southern California for some time.

Collection of urine specimens from infants is always difficult. Urine containing phenylpyruvic acid that has been dried on filter paper gives a positive test with ferric chloride reagent even after several months. We have devised a simple method for collection of urine on filter paper which can then be tested for the presence of phenylpyruvic acid. Mothers of newborn infants are given several pieces of absorbent paper and instructions to place the paper in their baby's diaper to become wet. The paper is taken out, dried, and mailed to us for testing. The test should be performed at 4 to 6 weeks of age, since phenylpyruvic acid may not be present in urine of infants with phenylketonuria until two to three weeks after birth.

When each paper containing dried urine is received, it is tested with a small drop of 10% ferric chloride solution. A urine specimen which contains phenylpyruvic acid turns green immediately. The green color fades after five minutes. The aromatic odor resulting from phenylpyruvic acid that has been dried on paper is very striking.

In any instance in which the ferric chloride test is doubtful or positive, the urine is examined further for the presence of ortho-hydroxyphenylacetic acid. This substance is excreted in large amounts in urine of persons with phenylketonuria and is as characteristic of the disease as is phenylpyruvic acid, though not so easily detected. This is done very simply by cutting out a 0.5-in. square from the paper containing the dried urine. This small paper is stapled 1 in. from the bottom of a piece of chromatographic filter paper 7 in. in height. The chromatogram is formed into a cylinder with the

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From the Department of Pediatrics, College of Medicine, University of Cincinnati, and the Children's Hospital Research Foundation.

urine paper on the inside to insure contact between the two pieces and placed in a solvent mixture containing isopropanol-ammonia-water (8:1:1) for six hours, or until the solvent mixture reaches the top. Then the chromatogram is removed, dried, and sprayed with a mixture of diazotized sulfanilic acid and sodium carbonate.

In phenylketonuric urine an orange spot of ortho-hydroxyphenylacetic acid appears approximately 4 in. above the position where the urine paper is stapled to the chromatogram. In normal urine no spot is seen. Aspirin and acetoacetic acid, which may interfere with use of the ferric chloride test on the original urine paper, do not interfere in the chromatographic detection of ortho-hydroxyphenylacetic acid.

This simple technique has been used to test urine of infants in the Cincinnati area. It was also used to test urine of a child with phenylketonuria during treatment with a phenylalanine-low diet. Dried urine papers were mailed to us for several days prior to and after institution of treatment. The papers collected before and during the first four days after the beginning of the diet had a strong odor of phenylpyruvic acid and gave positive tests with use of ferric chloride reagent. When small portions were excised and chromatograms prepared as described above, ortho-hydroxyphenylacetic acid was found. On subsequent days the papers containing urine gave no reaction with ferric chloride, but ortho-hydroxyphenylacetic acid was detected until the sixth day after treatment was begun. The concentration of phenylalanine in serum of the phenylketonuric child was 22 mg. per 100 cc. prior to treatment and 2.5 mg. per 100 cc. 10 days afterward.

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This study was supported in part by a grant from the United States Public Health Service, National Institutes of Health.

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COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. Kautz, M.D., *Secretary.*

FACTORS INFLUENCING CLINICAL EVALUATION OF DRUGS

WITH SPECIAL REFERENCE TO THE DOUBLE-BLIND TECHNIQUE

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and
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The fallibility of enthusiastic claims for new drugs makes it desirable to recognize those investigations which are likely to yield substantial data and to lead to interpretations that can be ascribed to pharmacodynamic effects rather than to wish, prejudice, coincidence, accident, or error. Some new drugs, despite statistical validations in reports of their efficacy and safety, do not survive the test of actual use or, even worse, have serious repercussions. The undesirable effects of such drugs employed therapeutically already have achieved alarming proportions, being observed in approximately 5% of 1,000 consecutive recent admissions to a major hospital in the city of New York.[1] This situation may become even worse if the present rate of development of new drugs continues (about 550 new preparations each year or more than one every day[2]) and if the medical profession continues to be misled by poorly conducted or inadequate evaluations of new drugs.

Criteria for distinguishing substantial studies from the unsubstantial must, therefore, be established in order to deal with the enormous number of reports on the large number of entirely new pharmacologically active drugs introduced in the market each year. Many methods for the evaluation of drugs have been designed. Of all the devices to insure valid data, none seems to have attracted

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so much attention and to have evoked so much controversy as the so-called double-blind technique. So much has been said and written about the technique that it does not need detailed description here. Briefly, it is a control device to prevent bias from influencing results. On the one hand, it rules out the effects of the hopes and anxieties of the patient by giving both the drug under investigation and a placebo of identical appearance in such a way that the subject (the first "blind" man) does not know which he is receiving. On the other hand, it also rules out the influence of preconceived hopes of, and unconscious communication by, the investigator or observer by keeping him (the second "blind" man) ignorant of whether he is prescribing a placebo or an active drug.[3] At the same time, the technique provides another control, a means of comparison with the magnitude of placebo effects.

The device is both philosophically and practically sound. In addition, perhaps because of the widespread attention it has attracted or the magic quality it appears to have, the double-blind technique has been assumed to be a complete method of drug evaluation in itself. Indeed, it is often called the double-blind test. Many seem to believe that all that is necessary for a good clinical study is to use it, and, since it is relatively easy to apply, many are exploiting it in just this way. A large number of papers emphasize in the very title that this type of control was used,[4] not only as if the use of a control in a clinical experiment were worthy of special mention, but also as if to warn the reader in advance that a special type of insurance had been taken out to guarantee that the results about to be recounted were beyond reproach.

If it were a fact that merely the use of the double-blind technique guaranteed the reliability of the data and the validity of the conclusions drawn from these data, the answer to the problem of drug evaluation would be simple indeed. But there are, in fact, a large number of studies in which the double-blind technique has been used, wherein the conclusions drawn from the data are open to question. In addition, the conclusions of some investigators are clearly at variance with well-established and universally accepted clinical and pharmacological observations. For example, the conclusions of one study imply that glyceryl trinitrate (nitroglycerin) has no clinical effects distinguishable from those of a placebo in patients with the anginal syndrome.[5]

That the double-blind technique does not rule out incompatible interpretations may be demonstrated by our own experiences in evaluating the analgesic action of aspirin. One of us (W. M.), using the double-blind technique, gave 25 patients with arthralgic pain aspirin in doses of 250 mg., 500 mg., and 1.0 Gm., three times a day. At the end of a two-week period, on each dosage, each patient turned in a report card indicating his own reaction to the medication during the period. This is a fairly common design for clinical evaluations in outpatients.

Statistical analysis of the data indicated that the patients were unable to distinguish between any of the doses of aspirin and the placebo (see table). Had five times as many observations been made, additional data of this sort would not have revealed a significant difference between reactions to aspirin and to the placebo. The results are inconsistent and without significant difference in any category for any treatment. These statistical analyses of the data could have been interpreted to prove that there is, in fact, no difference between the analgesic actions of aspirin and those of a placebo.

The double-blind technique was also applied by one of us (R. W. H.) to a different experimental design to evaluate aspirin, in which a bedside observer recorded the analgesic action as it developed.[6] Unlike the patients in the first study, who kept their own report cards and were seen only at infrequent intervals, the patients in the second study, who communicated immediately with an observer ("blind"), distinguished between the analgesic action of doses of aspirin and placebo and discriminated between graded doses of aspirin (fig. 1 and 2). These results were also highly significant statistically.

Response of Twenty-five Patients to Treatment with Aspirin and Placebo

Condition	Placebo	Aspirin		
		250 Mg.	500 Mg.	1 Gm.
Improvement, %	33	50	38	44
No change, %	33	19	33	31
Worse, %	25	31	25	25

How are we to resolve such discrepant results? No simple device such as the double-blind technique will correct astigmatism or myopia in the examination of drugs. The blind will not lead the blind to a valid conclusion unless the method somehow also provides vision.

It is our contention that the evaluation of the effects of drugs in man is by no means simpler, nor does it permit a less rigorous method of examination, than the formal experiment with the laboratory animal. The methodology has a strict discipline of its own. Clinical evaluations must deal appropriately with a complex of forces which affect patient reaction, or erroneous impressions of the virtues of new drugs will continue to be a source of confusion to the physician, of dangerous or ineffectual therapy for the patient, and of eventual economic loss to the manufacturer.

It is the purpose of this report to examine the factors which determine the sensitivity and the reliability of methods of drug evaluation in man and to consider the position of the double-blind technique in the schema. These factors have been analyzed elsewhere with, perhaps, less emphasis on the relative importance of double-blindness.[7] A variety of terms (response variables, primary stimulus variables, intervening stimulus variables[8]) have been used to describe these factors. To keep from beclouding the issues with yet more and, perhaps, equally unsatisfactory terminology, instead of ascribing terms to these factors, we shall describe them as stated in the following section.

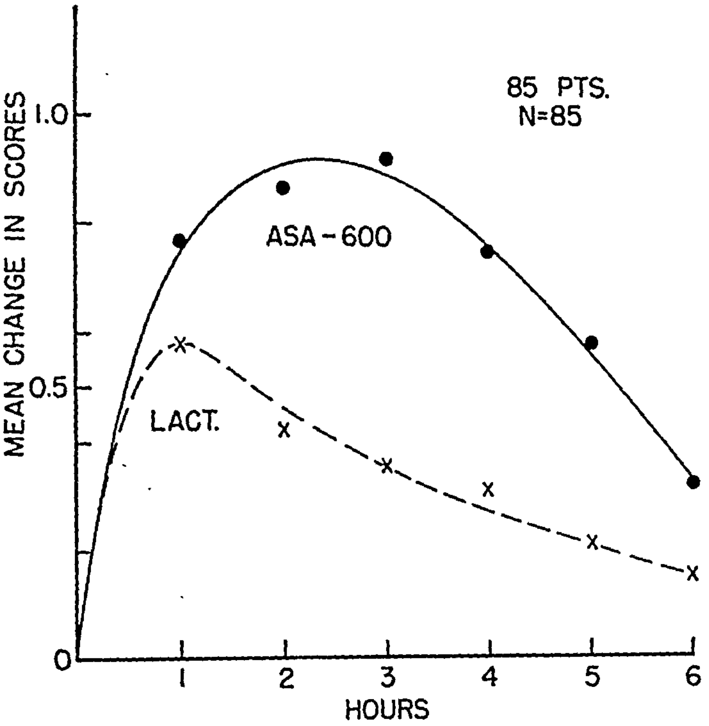

Fig. 1.—Time-effect curves for aspirin and placebo. Plot of mean hourly pain-relief scores, obtained in 85 patients with pain due to cancer, after oral administration of 600 mg. of aspirin and a lactose placebo. In these studies patients reported their pain to an observer in terms of "none," "slight," "moderate," and "severe." These categories were given numerical values, and pain relief was assessed as changes in score after administration of drug as compared with premedication score.

Forces Which Influence Data in Clinical Evaluations

The forces which may influence data in clinical evaluations, especially when subjective responses are involved, may be enumerated as follows: (1) pharmacodynamic actions; (2) dosage; (3) choice of subject; (4) use of controls; (5) collection of data; (6) sensitivity of the method; (7) placebo actions; (8) bias; and (9) forces extraneous to the experiment.

Pharmacodynamic Actions.—Pharmacodynamic actions present the least difficulty in their evaluation when objective measurement is feasible. When pharmacodynamic actions are potent, characteristic, and reproducible and are not seriously compromised by psychic forces, evaluation is thus relatively simple. For example, the action of a mercurial diuretic lends itself to precise, dependable, and relatively simple measurement, because it can be expressed in terms of the several pounds of fluid that a patient with congestive heart failure may lose overnight.[9]

Other drug actions, especially those which must be evaluated in terms of subjective response, are far more difficult to assess.[10] The influence of moderately potent analgesic agents on pain is difficult to evaluate, because pain is so susceptible to suggestion.[11] The hypotensive action of drugs is elusive because of the spontaneous tendency to wide variation of blood pressure in patients with hypertension, as well as because of the influence of immediate circumstance, tension, position, and rest on blood pressure.[12] Each drug effect, therefore, requires careful consideration in relation to the method used to measure it.

Dosage.—When the dosage is too low, regardless of the pharmacological actions or potency of a drug, clinical evaluation will not reveal a difference between placebo and drug. However, when too large a dose is used, therapeutic value may be obscured by toxic effects. Neither token nor toxic doses are useful in drug evaluations. Dosage must be carefully chosen. A dose should usually be used which, by preliminary experiment, is shown to lie in the sensitive portion of the dosage-response curve of the drug in question, although there are special situations and designs in which a threshold or a ceiling dose may be more suitable. As a matter of fact, the use of a series of graded doses provides a much more substantial basis for drug evaluation than the use of a single dose, no matter how well chosen, since it also serves as a built-in measure of

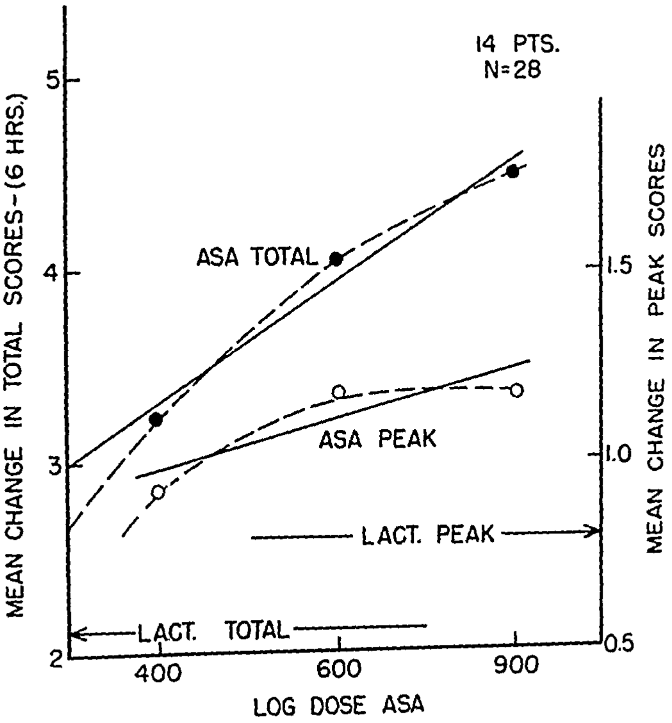

Fig. 2.—Dose-effect curves for aspirin. Mean peak relief scores (*right*) and mean total relief scores for six hours (*left*) are plotted against doses on a log scale. These were doses of 400, 600, and 900 mg. of aspirin and a placebo administered in a random order. Pain relief was assessed as in figure 1.

the sensitivity of the method and the discriminating powers of the study population—an internal control, so to speak.

Choice of Subject.—The choice of the appropriate subject is a critical matter in the design of clinical investigations. Just as some species of animals are more suitable than others for particular experiments in the laboratory, so some subjects are more appropriate than others for the clinical investigation of particular actions or effects. The argument that the patient for whom the drug is ultimately intended represents the best subject for the evaluation of a particular drug is a truism with serious limitations. Often he is the only possible subject, but there are also situations in which he may be unsuitable.[13] The choice of the subject, insofar as there may be a choice, depends more on the goals or aims of the investigation than on the disease for which the particular drug may be used if it is found to be active in man. The choice really rests on the purpose of the investigation, whether it is (1) to predict the value of a drug in the treatment of a particular disease, i. e., a therapeutic evaluation, or (2) to define the action of a drug in man, i. e., a pharmacological examination.

That there are two fundamentally different goals in clinical investigation is of obvious importance to those who design the investigations, but the realization of this distinction is of equal importance to those who read and interpret the reports of the investigation. It is too often assumed by readers, and even implied by authors, that the results of one type of investigation invariably apply to the other.

Some amplification may, therefore, be justified. The investigation of pharmacological actions of a drug in man is a necessary preliminary to its therapeutic evaluation. Although the results of the former may have implications of utility in particular disease states which are borne out by subsequent experience, sometimes the therapeutic evaluation fails to confirm the suggestive pharmacological findings. Only the therapeutic evaluation of the drug in the patient with the disease can provide the conclusive data of its value in the disease. The investigation of the therapeutic potential of drugs, therefore, cannot be carried out on any subjects but those with the particular condition for which it is proposed. If the evaluation is to have predictive significance, the group of patients must represent a fair (or random) sample of the patients who suffer from the disease.

The problem in the choice of subjects is a fundamentally different one, however, when the aim of the investigation is to explore or define the pharmacodynamic actions of a drug in man. Here the complex of unknown factors which influence the functional state of man may obscure the phenomena which are to be examined, measured, or evaluated. It is appropriate to avoid, eliminate, or reduce these unknown factors in the pharmacodynamic evaluation, since here the purpose is to define, within practical limits, fairly isolated drug actions. However, since these factors comprise everpresent issues in treatment, they must be accepted in the therapeutic evaluation of drugs.

Thus, while the utility of a diuretic in the treatment of congestive failure can be predicted only after an experience with a representative sample of patients with congestive failure, the effects of diuretics on particular electrolytes or in the influence of electrolyte load on diuretic action can be much better explored in healthy subjects. This is not to say that the healthy or normal subject is always the best for the pharmacological investigation. There are situations, e. g., that of the drug for cardiac arrhythmia, which demand the patient for the pharmacological as well as the therapeutic investigation. There are also situations in which there appears to be a choice, depending largely on the experimental approach, convenience, and availability of subject material. For example, drugs used in motion sickness can be investigated in voyagers with motion sickness aboard ship, and they can be investigated in healthy subjects with vertigo induced by the Barany test. Additional examples will not serve to clarify further the idea that, in the exploration of pharmacodynamic action of drugs in man, there are situations which are highly specific and in which only the patient with the disease for which the drug is intended can be the subject, that there are drugs for which both the patient and the normal man are suitable subjects and for which the choice may be based on convenience alone, and, finally, that there are situations in which the normal man appears to be clearly the more desirable subject than the patient.

The aforementioned considerations determine the type of subject essential for the clinical evaluation. Provided that they do not conflict with these, there are some general considerations which must also be taken into account. Subjects must be selected in a manner which insures the ability of the group, as a whole, to discriminate between "active" and "inert" agents. If this basic requirement for a useful method of drug evaluation is satisfied, unless there is a special reason for doing otherwise (e. g., the examination of a drug to be used only in infants), the attempt should be made to have the composition of the group as representative as possible of the general population.

To attain this objective, when extremely large numbers do not provide it by chance, some selection may be justified or even essential. Subjects likely to give misleading results should not overwhelm the group. The composition of the group with respect to age and sex should not be unusual. The potentially high side-effect liability of patients with renal disease and of the elderly, in general, must be considered. That dosage response in the very young sometimes differs significantly from that of adults must also be taken into account. Exceedingly phlegmatic subjects render the method less sensitive, just as highly neurotic and highly suggestible patients tend to compromise the sensitivity of the method through wide swings of mood and attitude as well as of placebo reaction (both positive and negative). The number of these subjects, therefore, should not be excessive.[14]

Knowledge of participation in an experiment, in the exploration of a new drug, or in any kind of a special examination places special psychic pressure on the patient and tends to make him act in something other than his usual manner—to be overly introspective, to help the investigator in some cases, and to react with fear in others. Some patients will tolerate discomforts with less difficulty when they know they are participating in an investigation; on the other hand, some may resent it.[15] But, however they react, this kind of information alters the subject and, thereby, adds a distracting influence to patient reaction with which the method of evaluation has to deal.

The acquisition of subjects for studies is an important practical problem, often a serious one. It would appear not only proper, but also legally desirable, to call on volunteers. However, the volunteer may present a problem in clinical evaluations; the highly cooperative and willing volunteer may provide a highly personal set of psychological problems which disturb the study. In an interesting analysis of this problem by Lasagna,[16] it has been shown that the volunteer is by no means representative of the average subject.

Use of Controls.—No experiment in any discipline can be pursued without controls. As a matter of fact, even those experiments which the experimenters, themselves, presume are without controls are, nevertheless, controlled. The control is a basis of comparison, and, thus, there is a control inherent in every judgment on a drug. The only important question about the control is, therefore, not whether it is present, but whether it is sound as a basis for the comparison on which the judgment is based.

It is tempting to use an easy way out, to use what has been called the historical control,[17] i. e., a recounting of previous or personal experience or recorded experience as a basis of comparison. Often, this is not recognized as a control—and with good reason, for it is a treacherous control. No method of drug examination is more likely to lead to erroneous conclusions, because it has none of the safeguards provided by other controls, the elimination of placebo effects and of bias. It also fails utterly to provide comparable bases for examinations of control and experimental groups. Only in the case of the disease in which an irrevocable or unquestionable characteristic course has been established, and particularly when the disease is rare, is the historical control justified.

The classic experiment uses separate groups for control and treatment, but this provides significant data useful for statistical validation only when the groups are extremely large or extraordinarily homogeneous. In man, this poses a serious practical problem. Since sets of identical twins (the equivalent of litter mates in the laboratory) are too rare to be hoped for, proper and careful matching (often an insuperable task) of control and experimental groups is essential. When the number of subjects is very large and when alternate patients are put in each group, chance alone will insure a proper balance. However, even when large numbers are available, the proper segregation of groups of patients is often a serious and difficult matter.

An alternate method, which is acceptable, is to give each patient the medicaments and the placebo serially, so that each subject serves as his own control. Since here the control and the experimental subject are identical, there is a valid basis for comparison. For such a comparison, the subject must be available for observation for a relatively longer period of time than that required in the first plan. In clinical evaluations, the second plan usually is more satisfactory than the first because smaller numbers are needed; hence, the study can be conducted in less time and with less cost. On the other hand, when the subjects have progressive disease, it may be inappropriate to compare effects at two stages of the disease. If this is the case, only separate control and treated groups are acceptable.

Collection of Data.—When objective measurement is possible and differences can be expected to be large, there is relatively little difficulty in collecting data. However, when the patient must communicate his experience, it is quite another matter. There are few experimental procedures in which so vital a part of an experiment as the collection, storage, and interpretation of observations is left in the hands of an interested, biased, and untrained assistant as that in which the subject himself is asked to report on his experiences after a period of medication. How can he help having his total recollection colored more by recent events than by those farther back in his memory—what happened two days or two weeks ago or even two hours before questioning—when, perhaps, he was annoyed by some action of the receptionist in the clinic.

The daily report-card system was designed to deal with this defect in the interval-report system.[18] When these records are kept by the patient himself, the improvement in methodology is more theoretical than actual. At the very best, it substitutes 24-hour recall for, say, two-week recall, but it still has the same fundamental deficiency. In practice, it is often no better than the longer interval system. We have observed patients fill out their "daily" report cards on their return to the outpatient department after an interval of as much as two weeks, immediately before being asked to turn them in. In any event, while it is obvious that it provides more data, the "daily" report-card system has not been subjected to an analysis which indicates that it also provides better data than the longer interval-report system. Other improvements have been suggested, such as having the subject mail a post card each night or phone a report each night,[19] but each of these compromises still leaves much of the data subject to the caprice of the patient for too long.

In general, any device which leaves the discrimination of reaction to drugs at the mercy of patient recall provides the setting for outside influence and tampering with the data. Every effort should be made to minimize the period between the experience with the drug and the recording of the data; the data should be taken out of the patient's possession as soon as possible and, thereby, kept as nearly as possible in its original form.

Sensitivity of the Method.—As in methods for chemical analysis, every method of drug evaluation requires a demonstration that its sensitivity is appropriate to the problem. A scale of sensitivity should indicate, first, the ability of the method to detect the drug action and, second, its capacity to discriminate increments in effects. Without the first, a negative answer cannot be defended, and without the second, a positive answer has no quantitative meaning.

A method of clinical evaluation can defend a negative answer only if it demonstrates at the same time that it appreciates the effects of a standard similar drug. The ability of a method to discriminate increments in effects can be indicated by its capacity for dosage response when a series of doses of the standard or experimental drug is used. Such a scale of sensitivity gives positive results a quantitative meaning.

The internal control just described is not only essential to establish the propriety as well as the sensitivity of the method as such, but it may not be eliminated in further clinical evaluations with the same method (as can be done with impunity in some other disciplines; e. g., methods of chemical analyses can usually be repeated many times without rechecking accuracy and sensitivity). The need for a continuing test of sensitivity comes not from instability of the method but from variations in the population of subjects, which at one time or another may make them more or less able to discriminate between "active" and "inert" agents.

Placebo Actions.—The term "placebo" has taken on many implications not within its original meaning. As the word is presently used in clinical evaluations, it includes a large series of visceral, somatic, and psychic responses resulting from the symbolic implications of the physician, his ministrations, and his medicaments.[20] Such actions are inherent in all medicaments, whether they are effective, excessive, hazardous, impotent, inert, unpleasant, inadequate, or inappropriate, as long as the medicament is prescribed by the physician for his patient.[21] To be certain that these are not the only effects due to drugs under examination, it is essential to have a basis of comparison of drug effect with "pure" placebo effect. To provide this, one must also give an inert medicament which is otherwise identical with the drug under examination.

It has been suggested by Gaddum[22] that for philological reasons such an inert medicament be called "dummy" rather than "placebo." But, dummy or placebo, an inert *control must be given in all studies to distinguish the difference between the effects of the act of drug administration and the pharmacodynamic effects of the medicament itself. This measure provides the only defense against the criticism that results reported are due to placebo actions.*

Bias.—The person of the physician and his medications have been shown to be symbolic forces of considerable potency in the relief of symptoms, the so-called placebo action. In addition, the hopes of the patient and the therapist, as well as any bias either may have with respect to treatment or experiment, also influence response to treatment. These must be reckoned with in all clinical evaluations.

The patient may want to get better to the extent that he is inclined to see good effects after administration of any new medicament. On the other hand, he may find compensations in his illness and wish to preserve his complaints and hence be inclined to see negative pharmacodynamic effects. "Toxic" effects from placebo are described in the literature,[23] the so-called negative placebo action.

The physician's knowledge of the nature of the medicament is exceedingly important, for, regardless of how much he tries, if he knows the identity of the medicament, he may well communicate this information to the patient. The importance of this unconscious (or conscious) communication has been proved by a study by Batterman and Grossman,[24] in which no difference between aspirin and placebo was detected by the patient unless the physician knew whether he was giving one or the other.

The standard and well-documented procedure is not only to use both placebo and drug which are *identical in appearance but also to keep both physician and patient ignorant of what is in use at the time of questioning, examination, and prescription,* i. e., the double-blind technique.[21a] *Both placebo and drug not only should look alike but also should* be prescribed and administered alike in order to prevent bias of both patient and physician from producing apparent drug actions. To be a real control, the placebo should also closely imitate the test-drug in any incidental effects such as taste, or other action perceivable by the patient or physician, but it should be independent of the action under question in the test.

This device, however, does not eliminate bias as an element in the method; it merely attempts to deal with it by equalizing its effects, so that unequally distributed bias alone will not fashion the apparently decisive evidence. At this point, it seems appropriate to emphasize that the double-blind technique is merely a control device; for that reason, we shall designate it the double-blind control.

Forces Extraneous to the Experiment.—The forces extraneous to the experiment include all external influences which affect the state of the subject's physical, functional, and psychic state—a change in the course of the patient's illness, a happy experience, a family quarrel, a change in the weather, or a turn of world affairs. To some extent, these factors may be reduced by removing the patient to the hospital, where they tend to remain relatively constant, compared with the relatively labile scene in the usual home under the best of circumstances. On the other hand, some patients may find the hospital environment disturbing rather than protective, and for them this change makes matters worse. The decision has to be made on an individual basis.

The tendency of extraneous forces to influence results can also be dealt with by prescribing medicament and placebo by a scheme of random distribution. Once again it may be pointed out that this device, randomization, does not eliminate disturbing external forces, but, by spreading the disturbing forces equally, in this way they favor neither drug nor placebo response.

Significance of the Data

It is usually good practice to plan the collection of data in such a way as to simplify subsequent statistical analysis, for, however the experiment is designed, the data should eventually be subjected to statistical analysis, if the significance of differences that are indicated by the data is to be established.[25] This is not to say that the mere statement of statistical significance insures correctness of interpretation. If the data are inappropriate or improperly collected, despite their statistical significance, their interpretation may be erroneous, as illustrated by the results of the study with aspirin cited previously.

It is well to remember that statistics prove nothing—they are merely a device for establishing the betting odds on the reproducibility of the results by mere chance. Statistical prognostication is always based on the assumption that the data used were worthy of collection; statistical analysis of poor data is tantamount to attempting to make a silk purse out of a sow's ear.

Interpretation of the Data

Of the several factors which enter into the design of a proper clinical evaluation, the current literature has placed overwhelming emphasis on one item, the double-blind technique, and relatively little on the others. Unless all factors are considered and afforded their proper importance in the design of clinical evaluations, improper and erroneous conclusions will be drawn from data that are supplied by studies which use the double-blind control just as well as from those which do not.

It is convenient to consider the design of a study for clinical evaluation in terms of a balance which is used to weigh the evidence for or against a particular pharmacodynamic or therapeutic effect of a drug as compared with chance occurrence. Which way the balance swings, i. e., whether drug action is favored or not, depends, of course, on the relative weight of the evidence in one or the other pan. Whether the swing is meaningful or misleading depends on whether the weight which swings it is due to a specific action of the drug or to any of a myriad of forces which influence man's behavior and his mental, physical, and visceral activity. When such a model is used, one way to prevent swings of the balance by factors other than the intrinsic pharmacodynamic action of the drug itself is to accept and spread their influence equally on both sides of the balance, thereby causing no disturbance in balance by their weight. This is precisely what is attempted by the control devices of double-blindness and randomization; they merely prevent chance and erroneous swings of the balance.

What is not often taken into account in clinical evaluations is how much weight is necessary to make the balance swing at all, that is, the basic sensitivity of the method. Whatever the original sensitivity, consider what is done with it in the usual design for clinical evaluation. Consider that such a balance is not empty at the outset of the evaluation, merely in balance; on both sides of the balance one places equally placebo action of drugs, bias, and influence of diverse extraneous factors, such as weather, political events, family stresses, and a number of other vagaries of human experience that tend to mold or alter man's functional state and his response to drugs. It is to be emphasized that these are not removed as interferences; they are permitted to remain. They are merely spread equally over both pans of the balance by the process of randomization and by the control of double-blindness. The balance is thereby deadweighted with a large amount of material which is immaterial to the specific problem at hand. No matter how sensitive originally, such a procedure makes the balance less sensitive, just as an analytic balance, sensitive to a fraction of a milligram under usual conditions, is no longer swung out of balance by milligrams when dead-weighted with several kilograms on each pan (fig. 3).

Ultimately, therefore, the sensitivity of a method of clinical evaluation is a function of the relative weight of the pharmacodynamic force under investigation and the weight of the nonessential interfering forces which are treated by equalizing them; the greater the former with respect to the latter, the more sensitive the method, and, vice versa, when the latter becomes relatively heavier, the method becomes proportionately less sensitive. The extent to which dead-weighting the balance grossly desensitizes the balance can lead to erroneous interpretations in the sense that the balance indicates no differences whenever it is used to weigh what it is no longer competent to detect.

Of the factors already discussed, some are subject to choice, such as the proper dosage range, the most sensitive subjects, and the appropriate control. Other factors may be modified. The removal of the patient from the home to a constant environment in the hospital may reduce the extraneous variables. The collection of data on the spot, rather than placing it in the hands of the subject himself (a procedure no investigator would ever dream of in any discipline other than psychiatry), reduces the treachery of patient recall. Finally, there remain some irreducible disturbances which can be neither removed nor modified, that is, bias, placebo actions, and the residual extraneous forces. For these there remain the double-blind control and the process of randomization to spread the prejudicial factors equally, so that none of them swings the balance in either direction.

We feel that in the studies with aspirin, which we cited briefly here, the reason for the discrepancy of results by the two methods used is to be found in their relative sensitivity. One method was insensitive because too many interfering forces were dealt with by the procedure of acceptance and balancing out to prevent prejudice of results, whereas the second was sufficiently sensitive because it had removed interference to a practical degree.

A great danger in interpreting clinical evaluations lies in failure to recognize the meaninglessness of the negative answer when the method is not sufficiently sensitive for the purpose. The failure to demonstrate statistically significant differences between drugs or treatments is frequently misinterpreted to mean that no real differences exist. However reasonable the latter may seem from the data, an assertion that the effects of the drug or treatment are identical cannot be proved. No statistical method is capable of, or designed to provide, such a prediction. If differences are noted in the data, statistical tests of significance can merely indicate the probability of their being due to chance. Thus, when the differences are statistically significant, one is assured that this is unlikely a chance occurrence, and one may then, with a measurable degree of confidence, rightly or wrongly (for the statistics themselves do not validate the basic data) ascribe the results to essential differences in the effects of the drugs. However, when the differences are statistically insignificant, a high probability of their being due to chance does not rule out the possibility that they may be real or even important. Such an occurrence could simply result from an inadequate trial or from an insensitive method of evaluation which statistical analysis may not indicate. Only when the design provides built-in controls, showing an ability to discriminate meaningful effects or to show graded effects of graded doses of the drugs, can any valid inferences be drawn from negative results (i. e., statistically insignificant differences).[26]

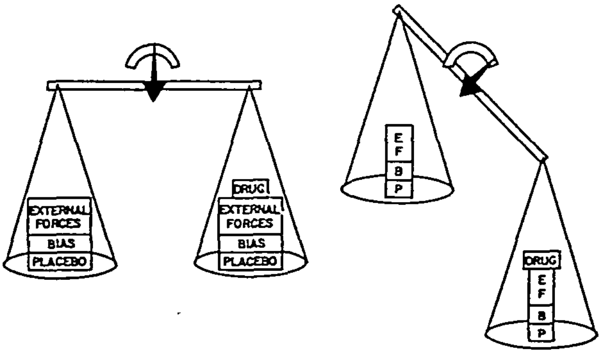

Fig. 3.—Diagrammatic representation of experimental designs for clinical evaluation. *Left,* excessive dead-weighting to prevent chance occurrence from swinging the balance reduces sensitivity to extent that drug effects do not swing balance and, hence, cannot be measured; *right,* reduced dead-weighting through appropriate design makes it possible to measure pharmacodynamic effects of same intensity with same balance.

The question arises whether the double-blind control must invariably be used in clinical evaluations. This has been reviewed by Gold.[21a] Much as we favor use of the device, occasionally it does not seem feasible. There are instances in which the drug promptly reveals itself by its unmistakable effect and automatically removes one or both blindfolds. How could one use the double-blind control in a study comparing a general anesthetic and a placebo? Page and Corcoran [27] point out that, although the physician may remain "blind," with many hypotensive drugs the patient's "blindness" soon vanishes because the drugs have obvious pharmacodynamic effects. Despite such difficulties, there are sometimes devices for circumventing them.

Conclusions

It is our categorical stand that, in addition to the use of the placebo control, the double-blind control should also be used whenever and wherever it is feasible. We conceive of no disadvantage in the application of the double-blind control—only protection against spurious data. It does not handicap design or reduce sensitivity, but it must be used to deal only with bias and psychic factors which cannot be eliminated. We also emphasize as strongly as possible that its use will not validate otherwise poorly designed experiments. When employed in a poorly designed experiment, it may prevent a false-positive interpretation, but it may also lead to a false-negative interpretation.

Each clinical evaluation must be sensitive enough to detect what it proposes to examine, and each experimental design must have built into it an indicator that it is capable of such detection. A negative conclusion is without merit unless a demonstration is incorporated in the clinical evaluation that the method is competent to indicate a positive effect when it is present, i. e., an internal control. It is suggested that in clinical evaluations another demonstrably effective drug always be used in addition to the placebo control to indicate this essential competence of the method.

Beyond this, there is the problem of the sensitivity of the method, the increments in effect which it can distinguish. Few clinical evaluations, indeed, indicate what differences in effect they can discriminate. Yet in all other disciplines of evaluation, it is standard procedure to provide such a scale. Clinical evaluations cannot escape this requirement; the complete method of clinical evaluation must incorporate such a built-in sensitivity scale through the use of graded doses, a demonstration of the increments in pharmacodynamic effect which the method can distinguish. When differences between standard and unknown or placebo are indicated, the sensitivity of the method to distinguish differences is thereby at hand, to indicate the quantitative significance of the differences.

Finally, we should like to state that the proof and establishment of the effects of many drugs, the proof of the superiority of one drug over another, require a plan which is based not only on the principles laid down here but which is also designed with due regard to the particular drug, the particular subject, and the particular circumstance under which the experiment must be conducted. There is as yet no standard method—there are only basic requisites, essential controls, and some well-established procedures—but each different pharmacodynamic action of a drug may need a different subject, a different control, a different circumstance, or a different design for its proper evaluation.

Investigations on which this report is based were supported, in part, by the Institute for the Study of Analgesic and Sedative Drugs, the Miles-Ames Research Laboratory, and the Sterling-Winthrop Research Institute.

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COMMITTEE ON MEDICOLEGAL PROBLEMS

THE PHARMACOLOGY AND TOXICOLOGY OF ALCOHOL

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This report is chapter 3 from a manual, being prepared by the Committee on Medicolegal Problems, dealing with medical and legal procedures involved in the use of chemical tests for intoxication.

Most of the drug effects of alcohol are due to its presence in the brain, since it is absorbed very rapidly and enters the brain within seconds after it appears in the blood.

The pharmacology of alcohol will be discussed in accordance with its effects on various organs and on certain bodily functions.

Effect on Body Organs

Skin.—Moderate doses of alcohol cause a marked dilation of skin vessels, resulting in a flushed face and hyperemia of other body surfaces. However, in alcoholic coma, the resultant impaired circulation causes a pallor of the skin. These two effects are of central origin.

Gastrointestinal Tract.—A temporary increase in the acidity of the gastric juice follows the ingestion of 4 to 10 cc. of alcohol, diluted to about 7% with water. This effect has been ascribed to the liberation of a histamine-like substance, or perhaps gastrin, by the action of alcohol on the gastric mucosa.[1] Experiments with isolated portions of the stomach and the duodenum showed that only the stomach antrum and the duodenum exhibit this response to alcohol, stimulating secretion in other parts of the stomach.[2] Intravenously administered, alcohol also causes an increase in the gastric secretion of acid, but whether this is due to alcohol in the brain is not known.

Concentrations of alcohol above 15 to 20% inhibit gastric secretion and may cause marked inflammation of the stomach mucosa. Vomiting frequently occurs after rather rapid drinking. Newman [3] has recently shown that the incidence of vomiting is practically the same after intravenous as after oral administration of alcohol, and it appears when the blood alcohol level reaches about 0.12%. This would seem to indicate that the emetic effect is also of central origin.

In the small intestine absorption of alcohol is so rapid that the concentration here rarely exceeds 1 or 2%. Except for a moderate, temporary increase in intestinal secretion, alcoholic drinks have very little effect on the gastrointestinal tract beyond the stomach.

Heart and Circulation.—Grollman [4] gave subjects 2.5 oz. of whisky and observed an increase of 5 to 10% in pulse rate, blood pressure, and total blood flow. These effects practically ceased in 30 minutes. He emphasized that these effects are mild, when compared to the action of many circulatory stimulants. Whether alcohol increases coronary blood

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flow is not entirely settled. Lasker and Sherrod[5] reported a marked augmentation of coronary blood flow of dogs after rapid intravenous injection of 50% alcohol. On the other hand, Russek and associates[6] could observe no significant electrocardiographic response in 12 heart patients who received 1 or 2 oz. of whisky before exercise.

Liver.—Josephson and Asplund[7] reported tests showing some impairment of liver function in one out of six healthy subjects, four hours after each had drunk 300 cc. of 40% alcohol. Forbes and Duncan[8] observed a marked drop in the liver glycogen level in rats receiving 3 Gm. of alcohol per kilogram, a dose corresponding to 18 fl. oz. of 100-proof whisky for a 150-lb. (68-kg.) person. They stated that administration of alcohol failed to restore glycogen in the livers of fasted rats. Sutherland and Watson[9] measured the output of urinary coproporphyrin III in subjects after a period of severe alcoholic intoxication. They reported a marked rise in this porphyrin level, lasting several days. However, this abnormality may not involve the liver. We will not attempt to discuss the question of the possible relationship between chronic alcoholism and liver cirrhosis.

Kidney.—The increased volume of urine after the consumption of alcoholic beverages is due both to the augmented water intake and also the marked diuretic effect of alcohol.[10] Alcohol inhibits the production of the antidiuretic hormone of the posterior pituitary. It appears unlikely that the moderate use of alcohol produces any kidney damage.

Effect on Central Nervous System

The most important drug effects of alcohol are those on the brain. The higher functions of the brain are inhibited first, with the more autonomic mechanisms affected later as the concentration of alcohol increases. Pharmacologists agree that the effect of alcohol on the brain is always a deterioration of function and never an improvement. This principle was first enunciated by the noted German pharmacologist, Schmiedeberg,[11] who stated:

> The subjective and objective states and manifestations, from which alcoholic drinks are considered condiments, are usually attributed to a stimulating effect of the alcohol.... However, a closer consideration of these manifestations shows that they are the results of a beginning paralysis of certain parts of the brain. Since this view was first expressed in the first edition of this work (1883), the idea that alcohol acts as a stimulant to the nervous system is no longer held in pharmacological circles.
>
> In the psychic sphere there is first lost the finer grades of attention, judgment, reflection, and ability to comprehend. This serves to explain the typical behavior of persons under the influence of alcoholic drinks. The soldier becomes more courageous since he observes the danger less, and reflects upon it less. The speaker is not tormented and influenced by the proximity of the public; he, therefore, speaks freer and with more animation. Ones self-appraisal rises greatly. Often one is astounded at the ease with which he expresses his thoughts and with the keenness of his judgment in matters which are beyond his mental sphere, when sober, and is later ashamed of this delusion. (Translation by author).

There are three serious types of impairment resulting from the depressant effects of alcohol on the central nervous system.

Less Efficient Vision and Hearing.—Tests of seven functions involved in vision were made by Newman and Fletcher[12] on 50 subjects before and after drinking. The blood alcohol levels of the subjects ranged from 0.058 to 0.218%, all but four being below 0.150%. At 0.115% and above, all subjects showed impairment in one or more of the tests. The highest incidence of impairment was in visual acuity, with 35 of the 50 subjects showing definite deterioration of this function. The number of the 50 subjects showing impairment in the other six tests ranged from 27 for eye coordination to 8 for side vision.

Using a flicker fusion test, Goldberg[13] reported that, with abstainers, reduced visual acuity begins at blood alcohol levels of 0.01 to 0.02%, with the threshold for moderate drinkers 0.02 to 0.03%, and for heavy drinkers 0.04 to 0.07%. In discussing these results he stated:[14]

> Alcohol had the same effect on vision as the setting of a grey glass in front of the eyes, or driving with sun glasses in twilight or darkness: a stronger illumination is needed for distinguishing objects and dimly lit objects will not be distinguished at all; when a person is dazzled by a sharp light it takes a longer time before he can see clearly again.

The effect of alcohol on binocular vision was studied by Brecher and others.[15] They used a procedure which caused momentary double vision without alcohol. After alcohol, the time required to attain single vision was greatly increased, being about doubled at 0.10% blood alcohol and quadrupled at 0.15%, when viewing at 20 ft. The authors stated, "somewhere between 0.05 and 0.10%, all subjects showed definite impairment." Charnwood[16] and Giardini[17] have also reported interference with ability to overcome double vision after the ingestion of 1.5 to 3 oz. of alcohol.

The effect of alcohol on hearing was tested by Hansen.[18] He gave five subjects 0.33 to 1.0 Gm. of alcohol per kilogram of body weight and reported an increase in the auditory discrimination threshold. This means that, after ingestion of alcohol, a higher tone intensity was required for the subject to perceive a given tone or to differentiate between tones.

Clumsiness of Voluntary Muscles.—The efficient transmission of nerve impulse from brain to voluntary muscle is impaired by the presence of alcohol in the brain and causes erratic muscular response. This impairment depends on the level of body alcohol and varies all the way from lessened efficiency in situations requiring intricate muscular coordination, through various stages of thick speech and staggering gait, to complete paralysis of voluntary muscles. Further rise in the concentration of alcohol in the brain also affects involuntary muscles, and may cause death by paralysis of respiration. The Harvard pharmacologist, Reid Hunt,[19] once said, "A fact frequently overlooked is that a person deeply intoxicated is near death and that a dose of alcohol slightly greater than that necessary to cause intoxication is a fatal dose." The fatal concentration of blood alcohol ranges from 0.5 to 0.9%, although lower concentrations have been reported in cases of fatal alcoholism.[20]

The level of blood alcohol at which beginning incoordination of voluntary muscles appears and the relation of the blood alcohol level to the degree of incoordination have been investigated by a large number of workers. These studies have measured the subject's efficiency in such operations as typewriting, handwriting, target practice, arm-steadiness, sway while standing, equilibrium in walking and standing, and speech. Other tests have involved the actual driving of a car or the use of a device simulating the operation of an automobile. The alcohol effect was always a lowering of efficiency, although the alcoholic subject frequently thought he was doing better than when alcohol-free. Goldberg[14] found that the threshold of impairment for the Romberg and finger-to-finger tests was a blood alcohol level of 0.05 to 0.10%, which levels, for a 150-lb. person, would mean a total quantity of body alcohol equal to the alcohol in 2 and 4 fl. oz. of 100-proof whisky respectively. A review of a number of extensive studies of this sort was recently published by Harger and Julpieu.[21]

Lengthened reaction time is one criterion of efficiency of muscular response. Alcohol in the brain causes a longer time lag before the voluntary muscle can obey the brain. Forbes[22] found that a blood alcohol concentration of 0.10 to 0.20% causes an increase of 10 to 30% in reaction time. At a speed of 30 miles per hour a car travels 44 feet per second, so that an increase of a fraction of a second in applying the brake may be a serious safety hazard in an emergency.

Deterioration of Judgment and Self-control.—Judgment and self-control belong to the highest functions of the brain. Such functions are impaired by lower concentrations of body alcohol than the levels which will inhibit the brain functions previously mentioned. Two results of impairment of these higher brain functions are euphoria and loss of inhibitions.

Euphoria: Euphoria means a hypersanguine condition of the subject. Although this phenomenon can hardly be measured quantitatively, all drinkers know that the consumption of two or three cocktails will cause them to "see the world through rose-colored glasses." Basically, this is the chief reason for the popularity of alcoholic beverages. While alcoholic euphoria may make a social gathering more enjoyable, may improve the appetite of a hypochondriac, and may tranquilize a victim of incurable disease, it is certainly contraindicated for an automobile driver. The driver should view his surroundings very clearly.

Loss of Inhibitions: The inhibitions are our moral brakes. The chief distinction between man and the lower animals is that the former exercises many more inhibitions. Without them he could hardly live a civilized life. The role of alcohol in lowering inhibitions is aptly described in the quotation from Schmiedeberg, given above. Concentrations of alcohol in the brain and blood far below those necessary to produce detectable muscular incoordination will cause a blunting of the sense of caution and normal restraints.

The driver or industrial worker who is a little "high" becomes a poor safety risk. He will take chances which he would avoid when alcohol-free. The added driving hazard due to concentrations of alcohol even below 0.10% is discussed in other chapters. The recognition that alcohol in the brain causes the subject to become more reckless is the reason for the definition of "under the influence" adopted by most courts and is what has prompted our railroads, airlines, and other industries to prohibit any drinking by an employee while on duty.

With some individuals, the loss of inhibitions caused by alcohol results in antisocial behavior. Seneca, the Roman philosopher and senator, wrote:[23] "Drunkenness kindles and discloses every kind of vice, and removes the sense of shame that veils our evil undertakings. For more men abstain from forbidden actions because they are ashamed of sinning than because their inclinations are good." The role of alcohol as an important causative factor in acts of violence has been repeatedly emphasized in recent, careful studies.[24]

The reasons why the central nervous system depression caused by even moderate concentrations of body alcohol is extremely detrimental to traffic safety have recently been very cogently stated by a special technical committee of the West German government:[25]

> The motor vehicle operator requires a sensitive perception-and-judgment ability for every unusual and unexpected moving change of the traffic situation within his sphere; he must literally anticipate the future traffic situation. Especially this ability to feel one's way in the traffic events is adversely affected with certainty at a blood alcohol concentration of 1.5 pro mille even in alcohol-habituated motor vehicle operators. Because of all this, no scientifically established facts are known, which permit assuming that driving fitness still exists above a blood alcohol concentration of 1.5 pro mille. (1.5 pro mille equals 0.15%.) (Translation by Dr. Kurt M. Dubowski, Iowa Methodist Hospital, Des Moines.)

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ABDOMINAL SURGERY IN THE AGED.—The over-all operative mortality in this series of [307] abdominal operations in patients 65 years or older was 16.6%, and this is considerably higher than the 2.1% mortality rate for all operations on the general surgery service during the same period. . . . The mortality rate for operations on patients between 65 and 75 years of age was 13.5%, and this increased to 23.1% for patients over 75. While coexisting disease in itself usually did not affect the mortality, the presence of uremia at the time of surgery was of ominous prognostic significance. The finding of azotemia should be evaluated carefully, for the outlook in the patient with increasing values for blood creatinine and urea nitrogen, in spite of adequate therapy, is indeed poor. It is doubtful whether any but obvious life-saving surgery is indicated in such a case. . . . The contrast of the nonemergency mortality rate of 11.1% and the emergency mortality rate of 26.8% is the most significant finding in this study. This disparity was noted in every category of surgical procedure carried out in the elderly patient. It varied from 1:5 for the upper gastrointestinal surgery to 1:1.2 for the colon surgery. . . . Most surgeons agree that there are certain factors of major importance if the mortality is to be minimal. These factors include restoration or maintenance of a normal blood volume, avoidance of infection, judicious use of antibiotics, control of fluids and electrolytes, and careful evaluation of coexisting disease. Attention to these details will allow one to perform surgery in the aged with optimism and enthusiasm. Only with such a sound physiologic approach can one truly believe that age is no contraindication to surgery.—L. F. Wilkins, M.D., and C. D. Knight, M.D., Abdominal Surgery in the Aged, A. M. A. *Archives of Surgery,* June, 1958.

COUNCIL ON INDUSTRIAL HEALTH

OCCUPATIONAL DERMATOSES—PREDISPOSING AND DIRECT CAUSES

This is the second in a series of reports prepared by the Committee on Occupational Dermatoses of the Council on Industrial Health, American Medical Association.

B. Dixon Holland, M.D., *Secretary*.

Occupational dermatitis continues to be the most frequently encountered industrial disease. This is best explained by considering the numerous factors that influence the susceptibility of the skin to eruptions caused by the occupational environment. These factors can be readily divided into two groups: (1) the innate or predisposing factors which determine the individual's cutaneous resistance and susceptibility and (2) the cutaneous challenges or direct causes presented by the individual's occupational environment.

Predisposing Factors

The cutaneous defense, or lack of it, against noxious agents is dependent to a certain extent on anatomic and physiological characteristics of the integument. These characteristics are sometimes tangible and obvious. At other times they are relatively intangible and obscure.

The tangible factors are the state of activity of the cutaneous pigment, sweat glands, sebaceous glands, metabolic disorders, and the intactness of the epidermis. All may influence the development of occupational dermatoses.

The amount of melanin pigment present in the skin is significant. Where it is present in large amounts, as in the Negro, cutaneous cancer and susceptibility to certain skin irritants are less likely.[1] It particularly protects against injury from ultraviolet light and heat.[2] Conversely, persons with fair or blond skin who have small amounts of pigment are more susceptible to light and heat stimuli than are persons with darker skin.

As the amounts of melanin may vary in the skin, similarly an individual's sweating capacity may be overactive or insufficiently active. If an overabundance of sweat is produced, the local areas so affected may become macerated, the skin surface pH may change, and, in some instances, pore closure may occur.[3] These conditions may predispose toward bacterial and fungus invasion and decreased resistance to external irritants. Excessive sweating can change a solid like calcium oxide to calcium hydroxide, which is an irritant when moist and in contact with the skin. If sweat production is abnormally low or absent, the individual tolerates excessive heat poorly and his tactile sensibility may be diminished.[4] Its lack also prevents the dilution of water-soluble irritants on the skin surface. Eccrine sweat excreted on the surface of the skin also assists in keeping the skin from becoming dry. A clinically dry skin is one which lacks water rather than oil. Thus, inadequate sweat production may lead to an abnormally dry skin.[5]

The exposed skin, except for the palms, soles, and ends of the fingers, is covered with an oily film produced largely by the sebaceous glands. The keratinizing epidermis and the apocrine glands also contribute to this lipid film which assists in maintaining adequate hydration of keratin.[6] Thus, the lipid film is partly responsible for keeping the integument supple and preventing chapping and fissuring. Further, it helps in protection against water and water-soluble agents, contains the precursor of vitamin D, contributes to the build-up of the acid mantle, and reduces the absorption of certain foreign substances. The lack of sufficient sebaceous excretion may lead to fissuring, infection, pruritis, decreased resistance to friction and pressure, and greater intolerance for fat-solvent chemicals.

An overabundance of sebaceous activity may produce a seborrheic state. This worker tends to be more susceptible to folliculitis, oil acne, and chloracne. An example of this relative intolerance is seen in the seborrheic worker with hairy extremities who, when exposed to insoluble cutting oil or heavy greases, is apt to develop comedones, folliculitis, and acne-like lesions. On the other hand, thick, oily skin has a greater tolerance for fat solvents such as naphtha, turpentine, and trichlorethylene.

Metabolic disorders may decidedly affect the skin's ability to maintain its integrity. Diabetes mellitus leads to increased blood and cutaneous glucose content which, in turn, may permit fungus and bacterial infections to occur more readily. The presence of metabolic or adolescent acne constitutes a disadvantage for the young machinist who works with cutting oils.

Ordinarily, the intact normal skin is impermeable to water and electrolytes, and this absorption barrier is presumably attributable to an intact stratum

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granulosum and stratum lucidum.[5] If this barrier is broken by pressure, friction, trauma, or other means, the skin becomes more susceptible to contact dermatitis, infection, and epidermal sensitization.

In addition to these rather well understood factors there are intangible factors which influence the skin's protective mechanism. Vasomotor instability, carelessness, lack of intelligence, and poor personal hygiene are a few of the background conditions which may make an individual worker more susceptible to skin disease. Of these, lack of personal cleanliness is undoubtedly the most common predisposing cause of industrial dermatitis.[1] Most cases of acute occupational dermatitis occur in young and new workers who are possibly less carefull and often fail to observe the suggested hygienic practices.

Preexisting dermatoses must be considered, since the patient with atopic dermatitis, lichen planus, psoriasis, or stasis dermatitis may prove to be unsuitable for many occupational endeavors. As a matter of fact, these nonoccupational dermatoses, and particularly any others associated with pruritis, usually lead to breaks in the skin surface, become aggravated by an industrial contact agent, and thereby become compensation problems. Preplacement examinations, carefully performed, can do much to facilitate the proper placement of the worker whose skin is unlikely to withstand the more hazardous jobs.

Classification of Actual Causes of Occupational Dermatoses in 41,628 Workers as Reported by Schwartz [1]

Material exposure	Incidence, %
Petroleum products and greases	18.8
Alkalies (and cement)	11.7
Solvents	7.8
Plants and woods	6.5
Metals and metal plating	6.0
Rubber and its compounds	3.2
Burns, physical and mechanical agents	3.2
Chemicals, unspecified	3.0
Paints, enamels, and varnishes	2.7
Acids and acid fumes	2.4
Dyes and dye intermediates	2.3
Chromates and chromic acid	1.7
Biological agents	1.3
Coal tar products	1.1
Furs and fur dyes and hides	1.0
Synthetic resins	0.9
Nonmetallic elements	0.4
Oils, vegetable (oils, fats and waxes)	0.2
All other known exposures	19.4
Unknown exposures	6.4

Sex is a factor in that women have a drier skin and are more susceptible to skin irritants. In spite of this, however, women do not suffer from severe occupational dermatoses as often as men. This may be due to less frequent employment in the more hazardous jobs, but, in addition, women tend to be more cleanly and they report skin irritations more promptly.

The second main group of predisposing factors are those which affect the worker's environment. Lack of proper ventilation, washing facilities, protective clothing, plant inspection, and prompt therapy are remediable conditions which unnecessarily contribute to occupational skin disease.

A clean and well-ventilated plant is more likely to be free of sensitizing and irritating substances. This is particularly true where noxious dusts, vapors, mists, or fumes are produced.[7]

Conveniently located washing facilities and frequent and adequate personal cleansing tend to prevent prolonged contact with substances capable of producing a dermatitis. Shower facilities for use after work may be necessary to reduce prolonged contact with severe cutaneous irritants. Efficient and mild skin cleansers should be readily available.

The difference that protective clothing can make is notable during hot summer months when workers tend to wear less protective clothing. This, in turn, results in a greater incidence of industrial dermatitis due to increased contact with irritants. Proper clothing for the worker, particularly in the presence of irritant chemicals, is an important phase of preventive medicine in modern industry. Not only should the clothing be adequate to protect the exposed parts, but it should be kept clean and changed as often as necessary to protect against harmful agents.

Protective ointments and creams are becoming more effective and more cosmetically acceptable. When wearing of gloves or other protective clothing is not practical, a protective ointment or barrier cream may serve as an aid in skin protection. Appropriate preparations may now be obtained to give limited protection against sunshine and some of the chemical irritants. One of the chief values of a protective cream is that the worker is more apt to remove it and any accumulated irritant by washing before eating and after work.

Periodic and thorough plant inspections, followed by indicated control measures, are necessary to reduce occupational hazards to a minimum. Such measures include education of personnel on how they may best protect themselves.

Medical attention for the worker with a dermatitis should be available. Acute dermatitis treated early is usually more responsive to therapy than a case that is allowed to become chronic. This situation is greatly simplified if the plant physician is well trained in industrial dermatology.

Overtreatment has been emphasized as a frequent factor in the prolongation of the clinical course of certain cases of occupational dermatitis.[8] An acute contact dermatitis will usually respond satisfactorily to local therapy, such as that with 1:20 Burow's solution (aluminum acetate) wet dressings and calamine lotion, along with control of the exposure. If stronger local preparations are used, the dermatitis may be severely aggravated. Dermatologists report that a high percentage of occupational skin diseases referred to them because of failure to heal actually represent cases of previous overtreatment. Common, basic dermatological principles are *sine qua non* in the treatment of occupational dermatoses.

Causes of Occupational Dermatitis

The table classifies the actual causes of the occupational dermatoses of 41,628 workers as reported by Schwartz.[1] Other similar analyses tend to approximate these figures.[9] These reports emphasize the importance of solvents, petroleum products, alkalis, acids, cleansers, and detergents and certain sensitizers in the causation of industrial skin disease. The definitive causes of occupational dermatoses have been classified into five groups: physical causes, mechanical effects, chemical agents, plant poisons, and biological agents.[10]

Physical causes are usually concerned with heat, cold, electricity, sunlight, x-rays, and radium. When the skin is exposed to abnormally high or low temperatures, the normal resistance to its environment may be impaired. Prolonged immersion of the worker's hands in water may produce maceration of the skin and predispose to infection or contact dermatitis. Exposure to abnormally cold temperatures may cause frostbite. Electric burns more often occur among those working as electricians and others not experienced with the exposure. Overexposure to sunlight may lead to sunburn and, if prolonged, can result in abnormal dryness, scaling atrophy, pigmentation, and sometimes epitheliomatous changes in the exposed areas. Blonds and redheads are more susceptible in this regard. Senile keratoses tend to develop into skin cancer, particularly if exposed to excessive active radiation. Overexposure to the radiation effects of x-rays and radium will result in varying degrees of radiodermatitis which can be highly serious since radiodermatitis is a premalignant lesion.

Mechanical effects result from friction, trauma, and pressure. The results produced by mechanical agents may vary from a simple callosity to a severe laceration or contusion. These areas may become more susceptible to fissuring, infection, and contact dermatitis.

The chemical agents cause the greatest number of industrial dermatoses. In 80% of cases the offending agent is a primary irritant and usually is an alkali, acid, or solvent. These can produce a dermatitis through direct local action if sufficient time and intensity of action are allowed. Less commonly the offending agent is a sensitizer. Some synthetic resins are examples. In cases of allergic dermatitis the initial contact with the skin does not produce notable changes outwardly; however, definite allergic changes do occur within the skin so that subsequent contact may lead to a dermatitis. Contact with coal tar, pitch, and certain petroleum compounds may produce photosensitization dermatitis and sometimes skin cancer after many years of exposure.

Many individuals become allergic to poisonous plants and woods. The most common example of the plant poisons is poison ivy. Other common offenders include cashew-nut shell oil, Japanese lacquer, poison sumac, and primrose. Some of the potent wood sensitizers include cocobolo, boxwood, mahogany, Brazilian walnut, rungus wood, cedar, redwood, satinwood, and cocus wood.

The biological agents that can produce industrial skin disease may be classified as bacterial, fungus, or parasitic. Erysipeloid among meat and fish handlers, actinomycosis among farmers, and grain itch among dock workers are examples of three classes of biological agents and the way in which they may produce occupational disease. Many other similar examples in industry could be cited, such as anthrax in hide and wool workers, monilial infection in kitchen workers, and cheese mite infestation among cheese handlers.

Summary and Conclusions

The most common industrial disease is occupational dermatitis, and it is largely preventable. The causes and predisposing factors which lead to the development of industrial dermatitis include, as the most important, lack of cleanliness. Contact with chemicals accounts for fully 90% of all industrial dermatoses. Eighty per cent of these are due to primary irritants, and the remainder are due to sensitizers.

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THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

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Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . "Medic, Chicago"

CONCORD OUT OF CONFLICT

ALL THREE branches of the organizational democracy of the A. M. A. have functioned separately but harmoniously in resolving a disagreement between some medical educators and medical practitioners.

The disunity arose when the Richmond County Medical Society hesitated to accept into membership any physicians who treated fee-paying patients at the University of Georgia's Talmadge Memorial Hospital while serving as faculty members of the university medical school. The society argued that these physicians were unable to control disposition of the fees and therefore they were taking part in the corporate practice of medicine. The hospital, in turn, contended that all fees went into its research fund and that compensation from patients able to pay was preferable to free service for them.

What makes this situation significant is that its handling by the medical profession illustrates the strength of the A. M. A.'s "three branches of government" as an effective constitutional democracy. These branches are similar to the United States system of democratic government, in that the policy-making House of Delegates corresponds to the legislative branch in Congress, the administering Board of Trustees is akin in concept and function to the executive branch centered in the White House, and the Judicial Council operates in the manner of the U. S. Supreme Court as a reviewing tribunal.

How did these three A. M. A. branches operate in the Georgia case? In June of 1956 the A. M. A.'s "legislative" House of Delegates (at the suggestion of the Committee on Medical and Related Facilities) recommended that, "on request of a medical society and a medical school, the American Medical Association's Board of Trustees establish, in cooperation with the Association of American Medical Colleges, a special committee whose function would be to investigate areas where there is friction between the medical school and the profession."

Little more than a year later this policy came to its first test when the Judicial Council was asked to rule on precisely such a friction. Six faculty members serving at the Talmadge Memorial Hospital alleged that the Richmond County Medical Society, by keeping them out, was in effect denying them membership in the A. M. A. and thus jeopardizing their careers. What did the Judicial Council do? Like the Supreme Court, it essentially upheld an action by the democratic system's legislative branch. The Council suggested that the Board of Trustees (executive branch) form a committee to help settle differences between the school and the medical society.

This was wisely done with the cooperation of the A. A. M. C. last April when seven physicians under the chairmanship of Dr. Leonard W. Larson, a member of the A. M. A. Board of Trustees, met separately (and later together) with representatives of the medical school and hospital, the state medical association, and the county medical society. The outcome is an agreement acclaimed by both sides. This pact recognizes that it is not the policy of the medical school or its hospital "to enter into the practice of competitive medicine"; favors the admission of "patients of unusual teaching interest" when referred by attending physicians (except in emergencies); and permits but does not require that fees (set by the attending faculty members) be deposited in a research fund of the hospital. A liaison committee of medical school and medical society representatives was created to resolve specific cases which could lead to controversy.

The A. M. A. committee's success can be attributed largely to the intense desire of its members to learn all the facts in the case, their willingness to travel to the scene and examine the issues in systematic detail, and their insistence on discussing only the germane data at business-like meetings (rather than stray to the emotion of unsubstantiated opinion at informal sessions). As one spokesman for the group commented later: "It may well be that this committee has established a precedent which may prove quite beneficial in the resolution of similar situations."

Much credit must be given to the committee who determined facts and objectively turned conflict into concord through direct negotiations with the parties concerned. Credit also belongs to the early members of the A. M. A. who foresaw the values inherent in the legislative-executive-judicial organization and so designed their constitution so that it might effectively represent the organized physicians of this nation.

THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Doctors, you have only two months to carry out one of the most important political tasks you have faced in the last decade.

I appeal to you to help elect United States senators and representatives who are dedicated to the promotion and strengthening of freedom and self-government and who support medicine's position against proposed legislation calling for hospitalization and medical care benefits for Social Security beneficiaries.

On November 4 the nation's voters will choose 32 senators and 435 representatives to the 86th Congress. The nominees for these top lawmaking offices now are beginning their campaigns and are seeking the support of their constituents. I urge you to talk or write to the incumbents and the challengers, explaining medicine's reasons for opposing legislation leading to government medicine via Social Security.

I believe we should thank sincerely those who are supporting our position and give them our solid backing on election day. Let us also explain our views to those who have not taken a stand on proposals to extend the federal government's control and direction over American medicine and the health affairs of the American people.

There is, of course, great political appeal in proposals to provide government-supervised hospitalization and nursing home care for the nation's 13 million persons eligible for Social Security benefits. But we know that such programs would offer less than the best medicine and that special privileges for a particular class of citizens soon would lead to demands by others for equal governmental largess.

If we as physicians are going to reverse the increasing federal control over health matters, we must act immediately. We must aid—within the law—in the election of legislators who oppose national compulsory health insurance. If such men and women are not elected, then legislation may be passed during the 1959-1960 session of Congress which would plunge the nation into a program from which there would be no hope of turning back.

We must support the right candidates and oppose their opponents. We must speak out publicly. And as the inspiring "Fighters for Freedom" pamphlet published by the American Farm Bureau Federation points out, we must "study, learn, help, write, serve, talk, work, organize, measure the candidates, register and vote for candidates" of our choice if we are to win our fight for freedom.

Political activity is for everyone. Therefore, I make this urgent appeal to each of you: Take the time during September and October to contact the candidates for the U. S. House and Senate and give them your views. Also explain to your friends and neighbors the real significance of legislation that would add medical service benefits to the Social Security program.

Remember that the issue is not merely the survival of the private-practice system of American medicine. It is really much larger; it is the possible loss of many individual freedoms, not just temporarily but forever.

I believe that we must have federal lawmakers in the 86th Congress who will stimulate and promote a climate in which private effort and ingenuity can exert their full effect. We do not need, or want, a "we'll-do-it-for-you" Congress. By your political activity and through your votes, you can help to make sure our nation is led by those who believe in guiding Americans, not in controlling them.

Gunnar Gundersen, M.D.
La Crosse, Wis.

ORGANIZATION SECTION

STATEMENTS REGARDING ENACTMENT OF H. R. 11414 AND DEPENDENTS' MEDICAL CARE ACT

June 27, 1958

The Honorable Lister Hill, Chairman
Committee on Labor and Public Welfare
United States Senate
Washington 25, D. C.

Dear Senator Hill:

I would like to take this opportunity to convey to you the views of the American Medical Association on H. R. 11414, 85th Congress. This bill, as passed by the House of Representatives, would amend the Public Health Service Act so as to authorize the Surgeon General of the United States Public Health Service to make grants-in-aid to schools of public health for the provision of comprehensive professional training and services.

The basic position of the American Medical Association with respect to Federal economic aid is one of opposition in those areas where private citizens, institutions, and local communities are capable of providing for themselves. In cases of demonstrated emergency, however, and as a temporary measure, we feel that Federal assistance may be justified.

For example, the Association believes that the financial situation of the nation's medical schools is sufficiently acute at the present time to warrant Federal assistance. We believe, however, that this assistance should be limited to a one-time grant, on a matching basis, and only for the expansion, construction and renovation of physical facilities.

As H. R. 11414 is presently written, it authorizes grants which could be used for staff and faculty salaries, operation and maintenance of facilities, and the acquisition of equipment. We do not believe that the use of Federal funds for such purposes, for what will undoubtedly be an indefinite period, is wise, since it could in our opinion, lead to the regulation and control of the public health schools by the Federal Government.

There is no requirement in this legislation for the Federal funds to be matched by the recipient schools, and therefore this desirable element of local responsibility is lost. Moreover, the bill does not contain any statement limiting or prohibiting Federal control over curriculum, administration, and admissions.

For these reasons, the American Medical Association is opposed to the enactment of H. R. 11414, 85th Congress. We urge your Committee not to report the bill favorably, and to make this letter a part of the record of the hearings on this legislation.

Sincerely yours,
F. J. L. Blasingame, M.D.
General Manager

Reproduced below is the statement of the American Medical Association before the Defense Appropriations Subcommittee of the Senate relative to the Dependents' Medical Care Act of 1956. Testimony was presented by Dr. Hugh H. Hussey (July 15, 1958).

I am Dr. Hugh H. Hussey of Washington, D. C., Dean of Georgetown University Medical School. I am appearing here today as a member of the Board of Trustees of the American Medical Association to discuss the medical care program for the dependents of members of the uniformed services. Since the inception of the program, I have been a member of the Department of Defense Dependents' Medical Care Advisory Committee.

As passed by the House of Representatives, Section 633 of H. R. 12738, 85th Congress, the Department of Defense appropriation bill contains a ceiling on expenditures which we feel could destroy the Medicare program. It appears from the printed hearings of the House Appropriations Committee that the inclusion of this section was recommended in an effort to force the Defense Department to care for more dependents in military medical facilities where, the Committee stated, the cost would be considerably less than in civilian facilities. Later in this testimony, we shall point out that it has not been established that military dependent medical care can be provided more reasonably than civilian care.

Officers in charge of Medicare have concluded that administering the program under the present language of the Appropriations bill would be extremely difficult, if not impossible. In any event, they report that the inclusion of the section would necessitate many major reductions in the benefits now offered to the thousands of dependents who live too far away from military bases to be cared for in military facilities.

As developed in the hearings, before Public Law 569, 84th Congress, was enacted, 40 per cent of dependents were not receiving any form of medical care provided by the government through the military program. Under the old program, therefore, there was a great disparity in the medical services being obtained by dependents of the members of the various uniformed services—indeed, even among dependents of members of the same service.

It was pointed out by representatives of the Department of Defense that this disparity in benefits contributed to the expensive and rapid turnover of trained personnel in the uniformed services. Recognizing this problem, Congress stated in Public Law 569 that "the purpose of this Act is to create and maintain high morale throughout the uniformed services by providing an improved and uniform program of medical care for members of the uniformed services and their dependents." This Committee has been advised by the Department of Defense that, to date, Public Law 569 has achieved its purpose, and the Medicare program has brought about a definite improvement in the morale of all uniformed personnel, particularly those who are married.

With some exceptions the American Medical Association has been pleased, in general, with the way the Medicare program has progressed since it began. We believe the program has been successful, in large measure, because representatives of the Armed Forces and the medical profession have cooperated closely and because dependents of service personnel have been permitted to choose freely between military and civilian sources of medical care.

The total number of dependents cared for in both military and civilian programs showed an overall increase of 39 per cent since the civilian program was enacted in 1956.

In the first 18 months of the program, less than half of the dependents were cared for in civilian facilities by private physicians. As reported in the House hearings, 43.6 per cent of this group resided too far from a military facility; 14.9 per cent required a type of care not available at the military facility; for 12.8 per cent the military facility was inadequate or overcrowded; 5 per cent required emergency care; the remaining preferred civilian facilities for diverse reasons, including those for whom civilian physicians or hospitals were more convenient.

The Department of Defense reported in the hearings before the House Appropriations Committee that of the dependents receiving care in civilian facilities, 41.4 per cent were maternity cases, 9.5 per cent gynecological conditions, and 22.2 per cent involved tonsillectomies. The tonsillectomies performed included a very large backlog which existed when the program was first enacted.

This same report showed that maternity and gynecological cases, according to several analyses of the Medicare program, constituted the major element of cost and frequency of utilization of both military and civilian facilities.

On the question of comparative costs of medical care for dependents in uniformed services and civilian facilities, it has been claimed in the House Appropriations hearings and before this Committee that medical costs in the civilian program are far greater than in the military. We know of no valid studies that have been made by the Department of Defense which accurately compare these costs. To our knowledge, the Department has no cost accounting system which isolates the cost of medical care for the dependent patient, particularly the total overall costs of maternity and surgical care.

This Committee's attention should be called to the fact that outpatient care is not authorized on the civilian side of the program except for emergencies and obstetrics, although outpatient care is authorized in military facilities. Hence the doctors' fees for surgery and deliveries, including pre-operative and post-operative care, and all outpatient care for obstetrics are charged against the per diem cost for a few days in civilian hospitals. For example, a physician's delivery fee would be pro-rated against a four-day hospital stay, or $31 a day for physician's services alone; whereas, he may have cared for this patient for nine months and will follow up the case later in his office—all for one fee.

Obviously, when the Air Force states that it can provide care for additional dependents on the basis of $10 per day, and the Navy for $16, which we must interpret to mean chiefly for obstetrics and surgery, they are not including outpatient pre- and post-natal and pre-operative and post-operative costs in arriving at these cost figures. Indeed, last year, as a result of similar claims made by the military services before the Appropriations Committees, the Bureau of the Budget, in reference to the cost of medical care in military facilities, stated in a letter of June 11, 1957:

> The military hospital operating costs include only direct costs, omitting many items of expense which, for budget and management purposes, need not be included in a Federal cost reporting system. The rate of $27.50 per day established by the Bureau of the Budget for the purpose of reimbursement between appropriations when dependents of one service are provided care in another service's hospitals does not reflect the true hospitalization cost to the Government.
>
> At least the following items of expense need to be added to arrive at an approximation of the full cost: depreciation of buildings and fixed equipment; outpatient care incidental to hospitalization; maintenance of a centralized procurement and depot system; maintenance of training facilities directed to increasing proficiency of hospital personnel; and management and professional direction by headquarters' staffs. While the Government is in effect a self-insurer against property and liability damages, such expenses cannot be excluded from a computation of total cost of patient care.

The Budget Bureau letter went on to say:

> There should also be included the costs of fringe benefits provided personnel. Such benefits for military personnel include free life insurance, medical care for the serviceman and his dependents, non-contributory retirement, as well as a number of minor benefits which are not susceptible to cost analysis. The Government also contributes toward the retirement and life insurance of its civilian personnel. While we have included certain of the fringe benefits in our computations, you can appreciate our concern that their costs not be regarded as definitive.
>
> Working with limited information and conceding that cost analyses of these expenses are not maintained, we have estimated that the above components of hospital expenses contribute the following approximate amounts to the cost per

patient day of providing care for dependents in military hospitals: depreciation, $1.25; outpatient care, $3.00; supply overhead, $0.45; education and training, $0.85; headquarters overhead, $0.20; liability and property insurance, $0.20; fringe benefits including life insurance, $1.70; medical and dental care, $0.45; and retirement, $0.50; total, $8.60. If these costs were added to the $27.50 uniformed service reimbursement rate, the total expense would approximate $36.

At the meeting on May 9, 1958 of the Dependents' Medical Care Advisory Committee to the Secretary of Defense, a representative of the Bureau of the Budget reported that a survey was being completed which would bring up to date the figures furnished last year. Since May, there has also been an additional cost factor to consider, based on the military and the civilian pay raises recently enacted which will affect the estimates for these costs for fiscal year 1959. These studies by the Bureau of the Budget have now been completed and indicate that the per diem cost for a dependent patient in military facilities will approximate $44. A copy of the Bureau of the Budget's letter of June 27, 1958 is attached for the Committee's information. I will appreciate your making it a part of the record.

Whether or not the cost is higher in a civilian facility, and we do not feel that it is, the program nevertheless has done what the purely military medical program could not do—it has cared for those dependents not residing near a military installation, others not residing with their sponsors, and those residing where adequate military facilities are not available.

It has always been our belief that any Dependents' Medical Care Program in the Armed Services should allow the dependent a free choice of physician and hospital, and should not be the basis for an expansion of military medical facilities. We have opposed such expansion of military medical facilities and military medical care activities because of the resulting necessity for the drafting of additional physicians under admittedly discriminatory legislation. In our opinion, if the present restrictions are retained in Section 633, both of these objectives would be defeated.

We feel that if the Congress sees fit to continue to provide, or to expand, medical care for the dependents of members of the Armed Forces, the services of civilian physicians and hospitals should be used wherever possible, to be paid for at prevailing rates, with provision for free choice of physicians. In our opinion, this is a sound, fair and workable position. It is one which has been tested and one which will benefit the service personnel and their dependents, relieve the unnecessary strain on the military medical services, and aid in the orderly development of community medical services for all of the people.

If the restrictions now in the bill are retained, there will also be a serious effect on service morale. In this connection, it should be remembered that the Dependents' Medical Care Act was instituted less than two years ago by the Congress primarily to attract and keep valuable personnel in the Armed Forces by giving them one of the fringe benefits that make business and industrial careers attractive.

This program, which is in the nature of a fringe benefit, whose purpose is to maintain high morale in the uniformed services and to encourage more men to enter and remain in a military career, should not be reduced or eliminated. We believe, with Secretary Brucker and the Department of Defense, that the action in setting a limitation on obligations for civilian medical and hospital care for dependents could cause the eventual destruction of the Medicare program.

It does not seem to us to be in the interests of national defense to destroy one program in order to save $30 million, while, at the same time, provide a military pay raise program costing $600 million when both programs have the same objective.

We recommend, therefore, that Section 633 be eliminated from the House Defense Appropriation bill.

REPORT OF JOINT COMMISSION ON ACCREDITATION OF HOSPITALS

The August, 1958, bulletin of the Joint Commission on Accreditation of Hospitals (660 N. Rush St., Chicago; Kenneth B. Babcock, M.D., director) is reproduced here for the information it contains that will be of interest to many physicians.—Ed.

Infections in Hospitals

The presence of infections in hospitals of various kinds will always be with us and we must accept it. To keep these infections to an absolute minimum is of paramount concern to all. This can be done only through continuous education and reeducation of all hospital personnel, to carry out known control methods with strict discipline at all times.

The Commissioners of the Joint Commission on Accreditations of Hospitals think that the matter is of such grave importance that they urge hospitals to study their own problem and set up systematic controls. The Commission cannot dictate what these controls should be. However, this Bulletin suggests an approach which might be used as a pattern. Each hospital should develop its own methods of study and control to meet its specific needs.

I. Committee on Infections:

The Commissioners recommend that every hospital have an 'Infection Committee' charged with the responsibility of investigation, control and prevention of infections within hospitals. Membership on this committee should include the medical staff, administration and nursing service personnel.

The member organizations of the Joint Commission are the American College of Physicians, the Amercian College of Surgeons, the American Hospital Association, the Canadian Medical Association, and the American Medical Association.

Where possible, participation with community health organizations such as health departments, medical societies and hospital councils is recommended, because the problem is not necessarily confined to the hospital itself. The responsibility of the committee can appropriately include the following:

- A. Establishment of definite controls. Control measures must have validity.
- B. Establishment of techniques for discovering infections on patients who have left the hospital:
  - 1. Trace source of infection for which a patient may be admitted.
  - 2. Periodic sampling by letter, card, call or visit of discharged patients.
- C. Make certain that bacteriologic services in or out of the hospital are available.
- D. Establish a system of reporting all infections among patients and personnel and keep records as a basis for studying the source of infections.

II. Review Existing Practices:

A. Clean and aseptic techniques should be practiced on all services of every hospital at all times. This includes the following procedures involved in patient care:

1. Re-check all dietary and food handling procedures, such as proper dishwashing techniques, preparation and disposal of food, refrigeration, sanitation of ice bins, and the disinfection of contaminated utensils and equipment. There should be a special technique for infected or 'isolation' patients.

2. Review laundry practices. This involves linen control, blanket control, special technique in handling and disposal of contaminated laundry in patients' rooms, nursery, operating room and the laundry itself.

3. Study carefully methods of handling and disposing wastes and excreta of sputum, feces and urine, and the environmental wastes of dressings, floor sweepings and food.

4. Re-study traffic controls and visiting rules in all areas, especially in operating rooms, nurseries and on obstetrical floors. They must be kept at an absolute minimum. Diligent maintenance of general cleanliness in all areas of the hospital, especially in service areas like utility rooms, janitors' closets, trash closets, etc.

5. Check sources of air pollution. Air conditioning and ventilating units should be inspected regularly for contamination through intake sources, screens and filters (wet or dry). Hospital floors and corridors must be considered as potential spreaders of infection. Wet mopping is far preferable to dry sweeping. There should be a definite practice established for the care and cleanliness of the mop after each usage; a dirty mop spreads infection.

6. Routine, periodic culturing of autoclaves and water sterilizers, which is a must for all hospitals.

B. Educate and orient all personnel in the practice of aseptic techniques. An informed worker is a better and a safer worker. It is especially important that physicians not consider themselves the exception to the rule, but both teach and set a good example for all. There can be only one accepted standard of practice. The following practices are some which should be studied:

1. Hand washing and scrubbing practices with review of proper soaps and detergents. Sinks with foot or knee controls in operating rooms, nurseries and isolation rooms are especially vital.

2. Proper gown techniques.

3. Proper mask techniques.

4. Proper dressing cart techniques and procedures.

5. Proper packaging of all goods, materials and instruments for steam sterilization.

6. Proper packing of autoclaves. No autoclave should be so tightly packed that the packages are either tight together or tightly pressed against the walls. It is especially important that all impervious containers such as cans, jars, test tubes and deep trays be so placed in the autoclave that they lie on their sides, or with the opening downward, which prevents the trapping of air and failure of sterilization at the bottom of the container. Improper packaging and improper packing by unskilled people can undo the finest autoclaving precautions.

III. Control Use of Antibiotics:

The medical profession has become increasingly aware of the problems created by the routine and indiscriminate use of antibiotics. Hospital surveys by the Commission reveal that the infection rate in most hospitals using antibiotics routinely is higher than in those not doing so. The common denominator in hospital infections appears to be the resistance of bacteria to antibiotics used on the individual case. From this, the conclusions drawn are that this increase in infections is due to the routine, indiscriminate use of preventive antibiotics in the absence of infection, and the indiscriminate use of antibiotics in the presence of infection without preceding cultures and sensitivity tests. In this latter type of case it is more than useless since without an adequate antibiotic, one may only inhibit the infectious agent and also at the same time stimulate the growth of other organisms which then become pathogenic.

IV. Recognize the Human Factor:

Any machine or equipment is only as good as the individual using it. All the rules, regulations and controls mean nothing if hospital personnel do not constantly check themselves for human errors. Continuing education and eternal vigilance in the cause, effect, and elimination of infections, in addition to instituting proper control methods, are important.

The recognition and elimination of infections in patients and personnel are thought by many to be the most important single facet in the control of infections. No hospital employee with a carbuncle, boil, acne, paronychia, fungus infection, upper respiratory infection, diarrhea, common cold, or in fact any infection, should be allowed in contact with patients. The reverse is true of infected patients. They must be isolated. One of the commonest avenues overlooked is by the physician not notifying the admitting office of the presence of infection already in the patient, or the admitting office or floor nurse not recognizing its very obvious presence on admittance.

There is no single factor responsible for so-called hospital infections. There are many factors and causes and each should be investigated. The Joint Commission cannot supply and does not have literature on special techniques and treatments. For specific articles refer to medical and hospital library indices on the subject.

AMERICAN ASSOCIATION OF MEDICAL ASSISTANTS TO MEET IN CHICAGO

The Second Annual Convention of the American Association of Medical Assistants (AAMA) will be held on Oct. 31, Nov. 1-2, at the Palmer House in Chicago.

The group will spend one entire afternoon visiting A. M. A. headquarters, where a program, a tour of the building, and a reception are being arranged for them. The American Medical Association has been working closely with this organization since it was organized in 1955. At the A. M. A. Clinical Meeting in November, 1956, the House of Delegates passed a resolution commending the aims and objectives of the American Association of Medical Assistants.

The AAMA is made up of men and women employed in the offices of doctors of medicine. It was conceived in Kansas City, Kansas, in the fall of 1955, by representatives from 15 states who were interested in establishing a formal organization to further postgraduate education. The constitution and bylaws were adopted at the association's second meeting, held in Milwaukee. The first annual convention of the AAMA was held in San Francisco, in October, 1957, just one "official" year after it was organized. The AAMA now has a membership of 6,000 from 17 states.

The program for the second annual convention includes a welcome address by Dr. F. J. L. Blasingame, Executive Vice-president of the A. M. A. and a symposium conducted by the physician-advisors to the group on such subjects as the value of the AAMA to physicians, the relationship of the medical assistant and Blue Shield, and professional ethics. The afternoon of the meeting's first day will be spent at the A. M. A.

Sections on business, technical, and medical subjects will be conducted simultaneously on the morning of the second day. In the afternoon, talks will be given by a clinic business manager and a director of a pharmaceutical company. The day will end on a social note with a reception, banquet, and installation of officers for the coming year.

The purposes of the association are: "To inspire its members to render honest, loyal, and more efficient service to the profession and to the public which they serve. To strive at all times to cooperate with the medical profession in improving public relations. To render educational services for the self-improvement of its members and to stimulate a feeling of fellowship and cooperation among the societies. To encourage and assist all unorganized medical assistants in forming local and state societies."

JOURNAL INDEX

The index to volume 167 of The Journal will appear in the Sept. 13, 1958, issue. Those who wish extra copies of the index may receive them, without charge, on request to the Order Department, American Medical Association, 535 N. Dearborn St., Chicago 10.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

AMERICAN BOARD OF ABDOMINAL SURGERY

The Council on Medical Education and Hospitals has received many inquiries from individuals who have been invited to submit applications for the Founders Group of the American Board of Abdominal Surgery. The inquirers have been concerned as to whether the American Board of Abdominal Surgery is approved by the Council on Medical Education and Hospitals.

Several years ago the Council was delegated the responsibility to act for the American Medical Association to grant approval to specialty boards which met appropriate requirements and standards. The Council on Medical Education and Hospitals continues to fulfill this function, assisted by the Advisory Board for Medical Specialties, which is composed of representatives from each of the approved specialty boards.

The American Board of Abdominal Surgery has not sought recognition from either the Council on Medical Education and Hospitals or the Advisory Board for Medical Specialties. It is, therefore, not approved by either of these groups.

MEDICAL NEWS

ALABAMA

Medical Progress Assembly in Birmingham.—The first annual meeting of the Medical Progress Assembly, sponsored by the Birmingham Academy of Medicine, will be held at the Tutwiler Hotel, Birmingham, Sept. 7-9. The program includes 16 papers, including "The Evaluation and Management of Pancreatitis," by Dr. Charles Wilmer Wirts Jr., Philadelphia, president, American College of Gastroenterology. Two panel discussions are planned: "Care of the Injured Patient," moderated by Dr. Champ Lyons, Birmingham, and "Atherosclerosis and Coronary Disease," moderated by Dr. Tinsley R. Harrison, Birmingham. At the banquet, 7:30 p. m., Sept. 8, with Dr. Paul P. Salter Jr., Birmingham, president, The Birmingham Academy of Medicine, presiding, Count Friederich Graf von Saurma, assistant to Wernher von Braun, U. S. Army Ordnance Missile Command, will speak on "You and Space." Question-and-answer periods and a ladies' program are arranged. The assembly has been approved for 16 hours of General Practice Credit, category I. For information write Dr. Samuel Buford Word, 2205 Highland Ave., Birmingham 5, Ala., General Chairman of the Assembly.

CALIFORNIA

New Hospital Started in Lennox.—Ground-breaking ceremonies for the $2,000,000, 100-bed Imperial Community Hospital, Lennox, have been held, with January, 1959, as the target date for occupancy. Being built in the heart of the airport industrial tract, in conjunction with the civil defense plan for Greater Los Angeles, the hospital is a step in the expansion program of the International Airport. The hospital will have a large rehabilitation section, under the direction of Dr. Stephen R. Elek, director of scientific research, which will be equipped for research in cardiac and peripheral vascular diseases, cardiovascular surgery, and in the diagnosis and treatment of outpatients in the cardiac and vascular clinics.

COLORADO

Fellowships in Pediatrics.—The department of pediatrics of the University of Colorado Medical Center, Denver, has announced the availability of fellowships in pediatrics in allergy, infectious disease, hematology, and premature and newborn nursery. Applicants should be graduates of approved schools of medicine and should have completed at least one or more years of hospital training. Preference will be given to those who are in the course of completing the pediatric hospital training required for the examination of the American Board of Pediatrics. The fellowships, for one or two years, include fundamental laboratory research and clinical investigation, as well as training in clinical diagnosis and management. Inquiries should be sent to Dr. Henry K. Silver, University of Colorado Medical Center, 4200 E. Ninth Ave., Denver 20.

MARYLAND

State Meeting in Ocean City.—The semiannual meeting of the Medical and Chirurgical Faculty of the State of Maryland will be held Sept. 11-12 with headquarters at the Commander Hotel, Ocean City. Registration and business sessions will be held the morning of Sept. 11 and the House of Delegates will meet the morning of Sept. 12. The scientific sessions will include an address by Dr. J. Sheldon Eastland, president of the faculty. Dr. C. Lockard Conley, professor of medicine, Johns Hopkins University School of Medicine, Baltimore, will present an illustrated talk on "Recognition and Significance of Anemia." Entertainment will include a clam bake luncheon and a dance. For information write Dr. Norman R. Freeman Jr., Medical and Chirurgical Faculty of the State of Maryland, 1211 Cathedral St., Baltimore.

MASSACHUSETTS

Hospital Seminar in Holyoke.—Dr. Arnold S. Relman, assistant professor of medicine, Boston University School of Medicine, and Dr. William B. Schwartz Jr., assistant professor of medicine, Tufts University School of Medicine, will conduct the semiannual Providence Hospital seminar Oct. 29 on "Fluid and Electrolyte Balance." Starting at 1 p. m., the program will run until 9:30 and will be held in the new hospital on Main Street in Holyoke.

Institute for Rehabilitation in Boston.—The $1,300,000 five-floor Rehabilitation Institute of the Boston Dispensary was formally opened in early May. The structure accommodates 23 house patients, with a daily outpatient load of 100. Patients make their own beds, prepare snacks in a practice kitchen, wash their clothes, if they wish, and go to the cafeteria for main meals. Started as a 10-bed

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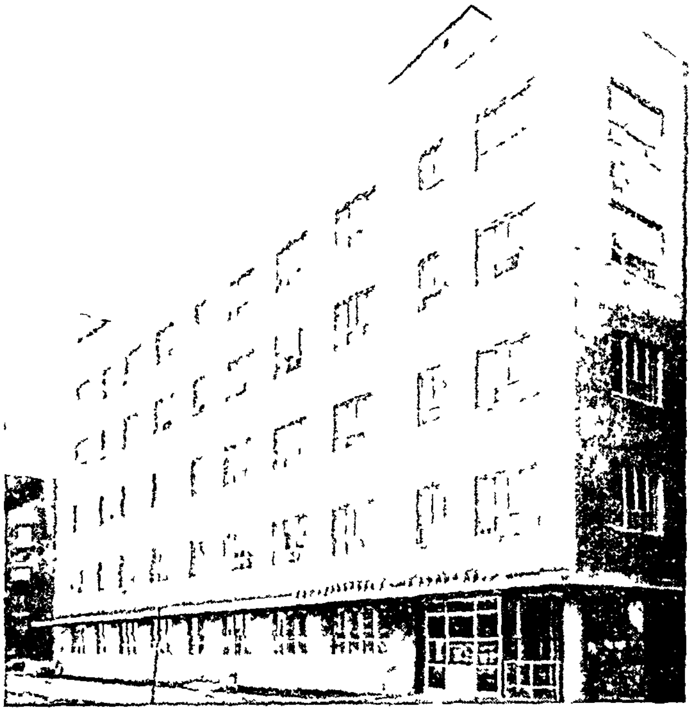
Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

pilot project in 1954, construction of the new institute began in October, 1956. Facilities include occupational, physical, and hydrotherapy areas, prevocational testing areas, plus recreation and T. V. rooms and roof-top sun deck. The institute was financed through awards from Massachusetts, Maine, and Vermont under the Wolverton Amendment to the Hill-Burton Act, totaling $400,000, community contributions of more than $800,000, and over $50,000 from the Junior League of Boston, Inc. The institute is administered by the Boston Dispensary, a unit of the New England Medical Center. Dr. John J. Lorentz is physician-in-charge. The fourth floor houses the new Arthur G. Rotch Rehabilitation Research Center. Edward H. Frieden, Ph.D., research coordinator, directs the basic and clinical rehabilitation research studies. Construction of the research center was partly financed through federal grants of $125,000.



Boston Dispensary's new Rehabilitation Institute.

Study of Stress Problems of Community Relocation.—A five-year study of the problems of relocation when homes are razed for industrial expansion and other aspects of the community life of persons now residing in Boston's West End area has been launched by the Center for Community Studies. Principal investigator is Dr. Erich Lindemann, professor of psychiatry at Harvard University and chief of the psychiatric service at the Massachusetts General Hospital, Boston. The study of social and psychological stresses involved is being made through a grant to the Harvard department of psychiatry at the Massachusetts General Hospital by the National Institute of Mental Health of the U. S. Public Health Service. The objective of the research is a study of the West End of Boston in the critical situation of relocation, including practical problems of planning and mental health and basic scientific issues concerning adaptation to stress and the social and psychological aspects of community life. The study will include a survey interview with a random sample of 400 resident families; both wives and husbands will be interviewed. Additional intensive interviews will be carried out with small groups of selected people to study special problems, including: family life, community life, adaptation to crisis, and the meaning of the physical invironment. Those questioned will be interviewed before moving and again, several years later, after moving. Two committees have been established: an advisory committee to help in guiding the research, and a citizens committee to aid in maintaining contact with the West End Community.

MISSISSIPPI

Dr. Gray Named State Health Officer.—Dr. Archie Lee Gray, for 20 years director of the Division of Preventable Disease Control of the Mississippi State Board of Health, became state health officer July 1. Eighteen months before, the Board of Health had named Dr. Gray assistant executive officer and secretary of the board, to groom him to take over the health post on the retirement of Dr. Felix J. Underwood. Dr. Gray began his public health service as director of Copiah County Health Department in 1930. When the Commonwealth Fund made an epidemiological unit possible in the Board of Health in 1933, Dr. Gray was called to organize and supervise it. In 1938 the unit was separated from the Division of County Health Work and developed into the Division of Preventable Disease Control and Dr. Gray was named director, a position he has held continuously. He is a diplomate of American Board of Preventive Medicine, and surgeon, inactive reserve, United States Public Health Service.

NEW HAMPSHIRE

Expansion Program at Dartmouth.—The Dartmouth Medical School has acquired $4,300,000 in new capital in the past year, Dr. Stephen M. Tenney, director of medical sciences, has announced. The grants include a $1,500,000 gift from the Rockefeller Foundation, $1,000,000 from the Commonwealth Fund, $1,000,000 from the U. S. Public Health Service, and $800,000 from the Ford Foundation. The educational plan at Dartmouth includes integration of three years of undergraduate liberal arts study with the first two years of medical school. The new curriculum provides elective periods during which medical students may take courses at the adjacent undergraduate college; or they may, if qualified, participate in a supervised research experience for as many as six months. The $4,-

300,000 thus far obtained is part of $10,000,000 in new funds sought for a new medical science building and endowment for the medical science faculty. The building will provide for a maximum of 100 students. During the past year the full-time, basic medical science faculty has been increased from 7 to 24. The expansion and revisions in the medical school's activities are being developed with the aid of a policy committee named by the trustees: Dr. George Packer Berry, dean of the Harvard Medical School, Boston; Dr. John P. Bowler, chairman of the Staff Board of Governors of the Mary Hitchcock Memorial Hospital, Hanover; Dr. Robert F. Loeb, professor of medicine, College of Physicians and Surgeons, Columbia University, New York City; Dr. Waltman Walters, senior surgeon at Mayo Clinic, Rochester, Minn.; and Dr. William Barry Wood Jr., vice-president of Johns Hopkins University, Baltimore.

NEW YORK

Department of Public Health Renamed.—Albany Medical College's department of public health henceforth will be known as the department of community health and there have been 17 new appointments to the teaching staff of the department, Dean Harold C. Wiggers, Ph.D., has announced. The change "reflects a greater emphasis on field study in Albany and surrounding communities resulting from curriculum changes adopted by the department within the past year." Under the change, Dr. Herman E. Hilleboe, State Health Commissioner and a member of the faculty of the medical college since 1948, becomes professor of epidemiology and community health. He formerly was professor of public health. Appointees include Dr. Thomas Hale Jr., director of Albany Hospital, and Dr. Victor N. Tompkins, assistant commissioner of health in charge of the division of laboratories and research in the state health department, both named associate professors.

Personal.—Dr. Anthony S. Bogatko, associate professor of clinical surgery, New York University College of Medicine, is the 1958 recipient of the Alumni Meritorious Service Medallion, bestowed by the Alumni Federation of the university. A bronze medal with the inscription "To Honor One Who Through Good Deeds Has Served Alma Mater" was presented to Dr. Bogatko June 4.——On May 27 New York Medical College, Flower and Fifth Avenue Hospitals conferred the honorary degree of doctor of humane letters on Dr. Willard C. Rappleye, retired dean of Columbia University College of Physicians and Surgeons, "in recognition of his long and distinguished leadership in the field of medical education." Dr. Rappleye was the commencement speaker.——Dr. John F. Moore Jr., who has served with Mutual of New York's Medical Department more than 30 years, has been appointed second vice-president and chief medical director, effective Aug. 1, succeeding Dr. Richard L. Willis, who is retiring after nearly 35 years with the company.

NORTH CAROLINA

Memorial Fund for Dr. Irwin.—A memorial fund honoring the late Dr. Henderson Irwin, of Eureka, has been set up within the Medical Foundation of North Carolina, Inc. The fund, to be known as the Henderson Irwin Memorial Fund, was established by a long-time friend of Dr. Irwin and will be used in medical education and research conducted under the auspices of the University of North Carolina School of Medicine, Chapel Hill. Dr. Irwin received his license to practice in North Carolina in 1914.

University News.—Dr. Michael Balint, consulting psychiatrist of the Tavistock Clinic of London, England, delivered the annual Phi Chi Medical Fraternity Lecture at the University of North Carolina School of Medicine, Chapel Hill, recently on "Opening Moves in Psychotherapy."——Dr. Robert W. Berliner, associate director in charge of research at the National Institutes of Health, Washington, D. C., gave the second annual Adam T. Thorp III Memorial Lecture at the University of North Carolina School of Medicine, Chapel Hill, on "Special Aspects of Renal Physiology." The lecture is given in honor of 7-year-old Adam T. Thorp, III, who was killed in an automobile accident summer before last. The child was the son of Dr. Adam T. Thorp, II, who graduated from the UNC School of Medicine in 1956.

NORTH DAKOTA

State Physicians Meeting in Fargo.—The 12th annual North Dakota regional meeting of the American College of Physicians will be held Sept. 6 in Fargo. The Veterans Administration, through the courtesy of Dr. Michael F. Koszalka, will provide the facilities of the VA Hospital's Auditorium for the meeting. Guest speaker from the college will be Dr. Howard Wakefield, of Chicago, who will present "Experimental Distention of the Human Gallbladder: Its Effect on the Electrocardiogram and Clinical Implications" in the afternoon and "A. C. P. Activities" at the evening dinner session. Dr. Raymond D. Pruitt, Rochester, Minn., will speak on "Certain Atypical Electrocardiographic Manifestations of Acute Myocardial Infarct." Registration fee is $10. For information write Dr. Reinhold O. Goehl, 221 S. Fourth St., Grand Forks, N. D., Governor of the College for North Dakota.

PENNSYLVANIA

Dr. Chapman Wins in Primary.—State Senator Dr. Leroy E. Chapman, of Warren, recently won the Republican nomination for State Senator, a post which he has held since his first election in 1930. Dr. Chapman was victor over Blain M. Mead in the district comprising Warren and Venango counties. The Senator never has been a loser in any campaign since his first in 1900, when he was elected president of Glade school board. Dr. Chapman has been chairman of the Appropriations Committee of the Senate of Pennsylvania since 1941.

Philadelphia

Dr. Wagner Named "Special Investigator."—The Hospital for Sick Children, London, has announced the appointment of Dr. Bernard M. Wagner as "Special Investigator" in their department of pathology for a three-months' period during 1959 to work with Dr. Martin Bodian. Dr. Wagner, pathologist to The Children's Hospital of Philadelphia, will go to Seattle shortly, where he will fill the Robert L. King Chair for Cardiovascular Research at the University of Washington School of Medicine. New techniques developed by Dr. Wagner at Children's Hospital under the auspices of the National Cystic Fibrosis Research Foundation will be utilized in the study of 200 cases of cystic fibrosis.

Dr. Crampton to Receive Award for Invention.—Dr. George S. Crampton, professor emeritus of ophthalmology, University of Pennsylvania Medical School, will receive an Edward Longstreth Medal from The Franklin Institute Oct. 15. The medal citation to Dr. Crampton reads: "For his development of the Borescope, a specialized periscope for the internal inspection of turbine shafts, rotors, guns and various closed vessels, by which flaws may be detected thus providing protection of vital importance from the physical and economic hazards of operational failure." The Longstreth Medal, founded in 1890 by Edward Longstreth, is awarded by the institute, Philadelphia's 134-year-old scientific-educational organization, "for inventions of high order and for particularly meritorious improvements and developments in machines and mechanical processes." In 1920, in response to a request by Westinghouse Electric Company, Dr. Crampton developed the first borescope in the attic of his Philadelphia home. That same year, he established the Lenox Instrument Company, to produce the instrument. Dr. Crampton also designed and made the first borescope for the Manhattan (A-Bomb) project. He was national president of the Illuminating Engineering Society in 1920-21 and was awarded the Gold Medal of the I. E. S. in 1956.

UTAH

Annual Meeting in Salt Lake City.—The 63rd annual meeting of the Utah State Medical Association will be held Sept. 10-12 at the Hotel Utah Motor Lodge, Salt Lake City. Dr. Reed W. Farnsworth, of Cedar City, president of the association, will open the program with an address. Two symposiums are planned, the first, sponsored by the department of pharmacology and moderated by Dr. Louis S. Goodman, Salt Lake City; and the second, "Treatment of Peptic Ulcer," sponsored by the department of surgery, University of Utah College of Medicine, and moderated by Dr. Walter J. Burdette, Salt Lake City. Guest speakers include Drs. Edward L. Compere, Chicago; Oscar Creech Jr., New Orleans; Peter H. Forsham and Ernest W. Page, San Francisco; Robert L. Jackson, Columbia, Mo.; Vincent C. Kelley, Seattle; John C. Krantz Jr., Ph.D., Baltimore; Petter A. Lindstrom, Salt Lake City; William T. Mustard, Toronto, Ontario; and Theodore E. Walsh, St. Louis. Movie sessions and exhibits are planned. At the president's banquet, 7:15 p. m., Sept. 12, Dr. Francis J. L. Blasingame, General Manager, American Medical Association, will be the speaker. For information write Mr. H. Bowman, 42 S. Fifth East St., Salt Lake City 2, Utah, Executive Secretary.

VERMONT

Dr. Daly Elected to Canadian Office.—Dr. John F. Daly, professor of dermatology at the University of Vermont College of Medicine, Burlington, and chairman of the division of dermatology at UVM, will serve as the vice-president of the Canadian Dermatological Association for the next year. Other officers elected at the association's 12th annual meeting were Dr. Robert P. Forsey, of Montreal, president, and Dr. Gibson E. Craig, of Montreal, secretary.

PUERTO RICO

Announce Appointments in Puerto Rico.—Recent appointments in the School of Medicine of the University of Puerto Rico, San Juan, include Dr. Edward Grzegorzewski, formerly director of the division of professional education, World Health Organization, Geneva, as head of the department of preventive medicine and public health, a vacancy which was created by the appointment of the former head, Dr. Guillermo Arbona as Secretary of Health of the Commonwealth. In addition, Dr. Ivan A. Pelegrina-Sariego has been appointed professor and head of the department of obstetrics and gynecology, the position left vacant since the death of Dr. Manuel Fernandez-Fuster. A new department of psychiatry has been created and Dr. Juan A. Rossello named professor and head of the department. Previously, Dr. Rossello was professor and chief of the section of psychiatry within the department of medicine.

GENERAL

Surgeons Plan World Tour.—The International College of Surgeons will hold its fourth around-the-world postgraduate clinic and lecture tour, beginning with departure from San Francisco Oct. 10. The return to New York will be on Dec. 3. The itinerary will afford an opportunity to attend specially arranged surgical clinics and demonstrations in most of the important cities to be visited. Sections of the College in Hawaii, Japan, Hong Kong, the Philippines, Thailand, India, Egypt, Turkey, Greece, Italy, and Spain will be hosts to the visiting surgeons at their clinics and hospitals. Information may be obtained by writing to Dr. Arnold S. Jackson, tour coordinator, 16 S. Henry St., Madison 3, Wis.

Otorhinologic Meeting in Chicago.—The American Otorhinologic Society for Plastic Surgery, Inc., will meet at the Conrad Hilton Hotel, Chicago, Oct. 12. Two evening panel discussions will be moderated by Dr. John T. Dickinson on "Otoplasty" and "Rhinoplasty." The program includes the following papers:

The Problem of the Naso-Frontal Angle in Rhinoplasty, Dr. Benito B. Rish, Brooklyn.
Deformities of the Chin, Dr. Edward C. Hinds, Houston, Texas.
Surgery of the Lower Lateral Cartilages, Dr. Samuel L. Lemel, Cleveland.
The Indication for Limited Rhydectomies, Dr. Morey Parkes, Los Angeles.

For information write Dr. Joseph G. Gilbert, 75 Barberry Lane, Roslyn Heights, N. Y., Secretary.

Conference on Insulin in Psychiatry.—An International Conference on the Insulin Treatment in Psychiatry has been arranged "to present recent advances in the basic aspects and the clinical uses of Sakel's discovery." There will be morning and afternoon sessions Oct. 24 and a morning session Oct. 25. This meeting, which is co-sponsored by Dr. S. Bernard Wortis, professor of psychiatry, McGill University, Montreal; Dr. Donald E. Cameron, professor of psychiatry, McGill University; and Dr. Jacques S. Gottlieb, professor of psychiatry, Wayne State University, Detroit, will take place at the New York Academy of Medicine, New York City. All interested individuals are invited. For information write to Dr. Max Rinkel, 479 Commonwealth Ave., Boston 15; or Dr. Andrew K. Bernath, 985 Fifth Ave., New York 21; or Dr. Harold E. Himwich, Galesburg State Research Hospital, Galesburg, Ill.

Announce Funds for Medical Research.—The Jane Coffin Childs Fund for Medical Research has announced appropriations made by its board of managers during 1957-1958 in a total sum of $276,087. The largest grants are as follows:

Lewis L. Engel, Ph.D., assistant professor of biological chemistry, Massachusetts General Hospital, Harvard Medical School, Boston; $67,590 for the three-year period (1958-61) for support of investigations of newer methods for the study of steroid metabolism in cancer.

Dr. Stanfield Rogers, research director, The University of Tennessee Memorial Research Center, Knoxville; $40,547 for the three-year period (1958-61) for support of investigations on the mechanism of action of the Shope papilloma virus in producing papillomas in rabbit epithelium.

Dr. Bengt E. G. W. Sylven, chief of laboratory, the Cancer Research Division of Radiumhemmet, Karolinska Hospital, Stockholm, Sweden; $30,000 for the three-year period for support of investigations on normal and malignant cells in various stages of growth and development; also a study of the possible release of enzymal proteins from malignant cells.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	Aug. 2, 1958		Aug. 3, 1957
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	..	..	1
New Hampshire	..	..	1
Vermont	..	..	..
Massachusetts	1	1	2
Rhode Island	..	..	..
Connecticut	1	2	3
Middle Atlantic States			
New York	5	11	15
New Jersey	4	7	5
Pennsylvania	3	4	7
East North Central States			
Ohio	..	5	23
Indiana	2	5	8
Illinois	2	5	20
Michigan	10	26	27
Wisconsin	..	2	12
West North Central States			
Minnesota	..	..	8
Iowa	1	4	2
Missouri	2	3	7
North Dakota	3	3	2
South Dakota	..	1	..
Nebraska	..	..	1
Kansas	..	..	5
South Atlantic States			
Delaware	..	..	..
Maryland	2	2	1
District of Columbia	..	..	6
Virginia	4	7	7
West Virginia	1	1	3
North Carolina	1	3	21
South Carolina	..	..	3
Georgia	..	..	3
Florida	1	5	3
East South Central States			
Kentucky	..	..	7
Tennessee	1	6	3
Alabama	5	5	2
Mississippi	1	7	7
West South Central States			
Arkansas	..	..	1
Louisiana	2	3	4
Oklahoma	1	8	9
Texas	10	16	23
Mountain States			
Montana	..	2	..
Idaho	..	..	1
Wyoming	..	..	1
Colorado	..	..	2
New Mexico	..	3	4
Arizona	..	1	1
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	2	..
Oregon	2	3	3
California	4	8	33
Territories and Possessions			
Alaska	..	..	..
Hawaii	3	3	..
Puerto Rico	2	2	6
Total	74	166	303

Tri-State Meeting in Shreveport.—The Tri-State Medical Society will meet in Shreveport, La., Sept. 10-11. The program includes the following:

Histoplasmosis, Dr. Harris D. Riley Jr., Oklahoma City, Okla.
Allergic Conditions in Children, Dr. Jack R. Anderson, New Orleans.
The Surgical Complications of Pregnancy, Dr. Isidore Dyer, New Orleans.
The Not So Simple Colles Fractures, Dr. Jack K. Wickstrom, New Orleans.
Cardiology, Dr. Don W. Chapman, Houston, Texas.
Surgical Treatment of Cardio-Vascular Disease, Dr. Denton A. Cooley, Houston, Texas.
Benign Disorders of Peripheral Nerves, Dr. Bertrum E. Sprofkin, Nashville, Tenn.

Exhibits are planned, and clinics and case presentations on pediatrics, orthopedics and obstetrics, and medicine and surgery are scheduled. A clinical pathological conference will be held the afternoon of Sept. 11, to be followed by the business meeting and a dove hunt. Registration fee is $10 for nonmembers. For information write Dr. Jason C. Sanders, The Sanders Clinic, 106 E. Kingshighway, Shreveport, La.

Annual Meeting of Obstetricians and Gynecologists.—The 69th annual meeting of the American Association of Obstetricians and Gynecologists will be held Sept. 4-6 at the Homestead, Hot Springs, Va., under the presidency of Dr. William F. Mengert, Chicago. The James W. Kennedy–Joseph Price Oration will be given by Dr. Roberto Caldeyro-Barcia, Montevideo, Uruguay, on "Hormonal Control of the Contractility of the Pregnant Human Uterus." Dr. Edward C. Mann, New York City will present "Habitual Abortion" as the Foundation Prize Thesis. Papers to be presented by invited speakers include:

Ferrodynamics and Pregnancy, Dr. Roy G. Holly, Omaha.
Pregnancy Subsequent to Ligation of the Inferior Vena Cava and Ovarian Vessels, Dr. Jason H. Collins, New Orleans.
Evaluation of Chemotherapy in Ovarian and Cervical Cancer by Tissue Culture Methods, Dr. John G. Moore, Los Angeles.
The Urinary Excretion of Interstitial Cell Stimulating Hormone During Normal and Anovulatory Menstrual Cycles, Dr. Francis M. Ingersoll, Boston.
Atypical Pelvic Pain in Women: Gynecologic-Psychiatric Considerations, Dr. Ralph C. Benson, Portland, Ore.
A Positive Cytology Registry, Dr. James H. Ferguson, Miami.

Entertainment includes the banquet Sept. 5. For information write Dr. Edward Stewart Taylor, 4200 E. Ninth Ave., Denver 20.

Society News.—The **American Goiter Association** has elected the following officers: president, Warren H. Cole, Chicago; president-elect, Edwin G. Ramsdell, White Plains, N. Y.; first vice-president, Virginia K. Frantz, New York City; second vice-president, Merritt P. Starr, Pasadena, Calif.; third vice-president, Benjamin M. Black, Rochester, Minn.; secretary, John C. McClintock, Albany, N. Y.; treasurer, Theodore O. Winship, Washington, D. C.; and executive councilor, John B. Stanbury, Boston (for four years). The next annual meeting of the association will be held in Chicago, April 30-May 2, 1959.——The **North American Chapter of the International Cardiovascular Society** has elected the following officers: president, Dr. Henry Haimovici, New York City; vice-president, Dr. Charles A. Hufnagel, Washington, D. C.; secretary, Dr. Paul T. DeCamp, New Orleans; recorder, Dr. Ralph A. Deterling Jr., New York City; and treasurer, Dr. Jere W. Lord Jr., New York City.——Officers elected at the annual meeting of the **American Rheumatism Association** include: president, Dr. Joseph J. Bunim, Bethesda, Md.; first vice-president and president-elect, Dr. Charley J. Smyth, Denver; second vice-president, Dr. Donald F. Hill, Tucson, Ariz.; and secretary-treasurer, Dr. Edward F. Hartung, New York City.——The **American Neurological Association** has elected the following officers for the coming year: president, Dr. Bernard J. Alpers, Philadelphia; president-elect, Dr. Derek E. Denny-Brown, Boston; first vice-president, Dr. Paul I. Yakovlev, Boston; second vice-president, Dr. Margaret A. Kennard, Ft. Steilacoom, Wash.; secretary-treasurer, Dr. Charles Rupp, Philadelphia; assistant secretary, Dr. William F. Caveness, New York City; editor of transactions, Dr. Rupp. The 84th annual meeting will be held at the Claridge Hotel, Atlantic City, N. J., June 15-17, 1959.

FOREIGN

Symposium on Intestinal Disorders.—The Royal Society of Medicine, London, will present a symposium on "Disorders of the Small Intestine (Excluding the Duodenum)," Oct. 31. Ten topics will be presented at the three sessions with Dr. Edward R. Cullinan, Mr. Harold C. Edwards, and Prof. Charles G. Rob as chairmen:

Investigation of the Small Intestinal Function.
Histopathology of the Small Intestine.
Jejunal Biopsy.
Radiology of the Small Intestine.
Polyposis of the Small Intestine.
Carcinoid Tumours.
Blind Loop Syndrome.
Massive Resection of the Small Intestine.
Medical Commentary on Disorders of the Small Intestine.
Surgical Commentary on Disorders of the Small Intestine.

A panel discussion will conclude the symposium under the chairmanship of Professor Rob. Admission is by ticket only. Overseas visitors should apply for tickets as soon as possible by writing to the Royal Society of Medicine, 1, Wimpole St., London, W. 1, England.

International Congress of Angiology in San Remo.—The III International Congress of Angiology will be held in San Remo (Casino Municipal), instead of in Venice as formerly announced, Sept. 24-28. The general subject, "Experimental and Clinical Pathology of the Peripheral Vascular Diseases," will be dealt with in five successive meetings. A symposium on experimental and clinical pathology of the lymphatics will be held in conclusion of the congress meetings. For information write to the Secretariat of the Congress, c/o Clinica Dermatologica, Universita di Pisa, Italy.

CORRECTION

The Impact of the Antibiotics on Medicine and Society.—In the review of the monograph of this title in The Journal, Aug. 9 issue, page 1893, the name of the editor should have been Iago Galdston.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

American Board of Dermatology: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Written.* Oct. 20, 1958. *Oral.* Chicago, Oct. 13-16. *1959 Schedule—Written,* Oct. 19. Final date for filing application is May 1. *Oral.* For candidates in the South and Southwest, New Orleans, Feb. 3-6. Final date for filing application is Jan. 1. *Oral.* For candidates in the Midwest. Chicago, April 15-18. Final date for filing application is Jan. 1. *Oral.* For candidates on the West Coast. Final date for filing application is March 1. *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application is March 1. *Examination in the Subspecialties. Gastroenterology.* Philadelphia, April 17-18. Final date for filing application is Feb. 1. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

American Board of Obstetrics and Gynecology: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written,* qualifying test (Part I), January 1959. Final date for filing application was July 1, 1958. *Oral Examinations 1958* (Part II): Chicago, Oct. 6-10. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications was Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

American Board of Otolaryngology: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

American Board of Pathology: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Plastic Surgery: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports was July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

American Board of Preventive Medicine: *Examination in Public Health.* St. Louis, Oct. 24-26. Final date for filing application was Aug. 15. Sec., Dr. Thomas F. Whayne, 3438 Walnut St., Philadelphia 4.

American Board of Proctology: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

American Board of Psychiatry and Neurology: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Regular Examination.* Washington, D. C., Dec. 8-11. Final date for filing application was July 1. *Special examination in Nuclear Medicine for those diplomates in Radiology or Therapeutic Radiology.* Washington, D. C., Dec. 6. Final date for filing application is Oct. 1. *Special Examination.* Cincinnati, Mar. 16-19, 1959. Final date for filing application is Nov. 1. Candidates completing training June 30, 1959 are not eligible for the Spring 1959 examinations. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Philadelphia, Sept. 15-16; Rochester, Minn., Oct. 20-21; Nashville, Tenn., Nov. 17-18; New York City, Dec. 15-16; Houston, Tex., Jan. 12-13; New Haven, Conn., Feb. 9-10; Durham, No. Car., March 9-10; San Francisco, April 13-14; Indianapolis, May 11-12; Columbus, Ohio, May 14-15. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: Various centers throughout the United States. *Written.* Spring of 1959. Final date for filing application is December 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Avenue, Detroit 2.

American Board of Urology: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles Wishard, Jr., 30 Westwood Road, Minneapolis 26.

GOVERNMENT SERVICES

ATOMIC ENERGY COMMISSION

Technical Exhibit.—The United States Exhibit for the United Nations Second International Conference on Peaceful Uses of Atomic Energy (Geneva, Sept. 1 to 13) complemented the American technical papers and film programs and presented to the conference and to the world a graphic demonstration of the high level of competence and vitality of American science and technology. The displays covered a broad technical front and were divided into four general sections: (1) basic sciences, (2) life sciences, (3) fission reactors, and (4) fusion research.

Highlights of the basic sciences section included displays of some of the recent developments in nuclear physics and chemistry, including the recently discovered catalytic action of the mu-meson in deuterium fusion, the production and identification of anti-nucleons, neutrino physics, and the failure of the conservation of parity in certain types of subatomic reactions. A large liquid scintillation counter in which the radioactive body content of exhibit visitors was measured was a popular feature of the life sciences section. The use of radioisotopes in research and in diagnosis and treatment of cancer, heart disease, and other medical problems was shown. Other displays of general interest included a study of photosynthesis, the biodynamics of metabolism, enzyme action, and milk production. Seven operating isotope laboratories were displayed. The fission reactors section included two operating research reactors. The Triga, a 10-to-30-kilowatt reactor was assembled to produce radioisotopes for use in other parts of the exhibit. The 10-kilowatt Argonaut training reactor was also in operation. To illustrate typical training and research projects, the Argonaut was assembled, tested, and put into operation during the conference. A full-scale model of the four-story high pressure vessel and core of the power reactor now producing electricity at Shippingport, Pa., was displayed. An operating simulator of the experimental boiling water reactor was also displayed. Scale models of other types of power reactors as well as a model of the N. S. Savannah, the nuclear-powered merchant ship now under construction, was featured. The thermonuclear or fusion research section was essentially a status report on the major paths presently being taken by U. S. scientists in pursuit of a controllable, sustained thermonuclear reaction.

AIR FORCE

Residency Training in General Practice.—Although the Air Force has entered the age of space, it still needs general practitioners. Approved residencies in general practice are available at the U. S. Air Force Hospital, Maxwell Air Force Base, Alabama, and certain civilian hospitals. The Air Force physician trained in general practice plays a dominant role in the successful accomplishment of the Air Force medical mission. He is the family physician whose broad general knowledge provides a balanced medical capability and whose close patient-doctor relationship with Air Force men and their families provides real Air Force dividends not measureable by statistics. The Air Force general practice residency program provides one year of training in medicine, including pediatrics and psychiatry and one year in surgery, including traumatic surgery, fractures, obstetrics, and gynecology. It is anticipated that programs will be approved by July, 1959, in additional hospitals at Andrews Air Force Base, Washington, D. C.; Keesler Air Force Base, Mississippi; and Wright-Patterson Air Force Base, Ohio. After completing residency training in general practice, medical officers may attend the primary course in aviation medicine if they so desire and are physically qualified. Physicians interested in an Air Force career in general practice may write directly to The Surgeon General, Headquarters, U. S. Air Force, Washington 25, D. C.

ARMY

Personal.—Brig. Gen. Clement F. St. John has arrived at Brooke Army Medical Center where he will assume command of Brooke Army Hospital, replacing Major Gen. Stuart G. Smith, who has been named commander of Letterman Army Hospital in San Francisco.

NAVY

First Commandant's Representatives' Seminar.—About 22 inactive reserve medical department officers attended the First Commandant's Representatives' Seminar at the Bureau of Medicine and Surgery, Washington, D. C., from Aug. 4 through Aug. 8. The seminar's purpose was to present a general review of the naval reserve, the training programs for undergraduate medical students, and selected phases of recruiting concerning the commissioning of medical department personnel. The reserve officers attending were faculty members of accredited medical schools throughout the United States.

VETERANS ADMINISTRATION

Retraining the Blind.—A decade of successfully retraining the blind to lead normal lives has been completed by the Blind Center located at the Hines, Ill., VA Hospital. This is the only center of its kind for the VA and the Armed Forces. It has helped 470 blinded veterans to "see" with walking canes, to overcome fear in doing ordinary things, to use power tools and appliances for the blind, and to become independent, useful citizens again. Honored guests at the ceremony marking the center's 10th anniversary were the 20 blinded veterans currently in residence for the 16-week rehabilitation course. Chief of blind rehabilitation activities since the founding of the center is Russell Williams, who was blinded by an exploding shell in France in World War II. His staff includes 4 instructors in Braille and typing, 16 orienters, 4 manual arts therapists, and a counselor. The orienters are specialists in teaching systematic habit retraining, especially in foot travel. The staff has training and experience in corrective therapy, which provides a good foundation on which to superimpose the special skill and philosophy of a rehabilitation treatment program for blinded veterans.

A typical day at the center includes orientation, Braille, typing, shop work, counseling, physical reconditioning, and group recreation. The recreation may consist of bowling, golf, and weekly dances. An integral part of the training is mastery of the "long white cane." With this cane, the veteran is taught to get about the hospital corridors and grounds. He soon branches out into nearby streets and finally he goes into Chicago's busy downtown section. One veteran said of the training: "Fear can destroy a man a little at a time. Fear of movement and fear to do ordinary things can injure his mental and physical health. After 16 weeks at the center, you lose that fear, and this is away above my expectations. The training is more protection for a blind man than a tank is for a soldier."

Foster Home Program.—The Veterans Administration's nationwide foster home program to provide a normal home life for recovering mental patients has greatly increased in the past two years. The total of 1,249 mental hospital patients living with their "adopted" families in private homes near the hospitals in 1957 is a 24% increase over the number in 1956 and a 56% increase over the number for 1955. The hospitals placed 639 patients in the homes during 1957 and reported 219 of those in the program recovered sufficiently during the year to be discharged from hospital rolls. Most of the veterans in the homes are over 40 years of age and had been hospitalized for many years. Placement in a foster home is the first step in their return to community life.

PUBLIC HEALTH SERVICE

Genetics Study Section.—A genetics study section consisting of a scientific advisory group of nongovernmental scientists has been formed by the National Institutes of Health, to handle the increased number of research grant applications dealing with genetics and to give appropriate recognition to this important, rapidly expanding discipline. In addition to reviewing and recommending action on these applications, the genetics study section is charged with the public health responsibility of surveying the status of research and training in the genetics field in order to determine areas in which additional activities should be initiated or expanded. The cell biology study section will continue to review and evaluate research grant applications dealing with basic problems of cellular structure at all levels of magnification as it responds to stimuli both intrinsic and environmental. The first meeting of the newly constituted study section will be held in September in Bethesda, Md.

Personal.—Dr. Sara E. Branham, internationally known bacteriologist, retired on July 31 from the National Institutes of Health, Bethesda, Md. For 30 years she has been engaged in microbiological research. An authority on the meningococcus, she demonstrated the epidemiological differences in groups of meningococci and played a major role in the development of the current classification of these micro-organisms. With the advent of the sulfonamides, Dr. Branham was one of the first to study the susceptibility of various micro-organisms to these drugs. She also devoted special attention to the toxin produced by Shigella dysenteriae. Since June, 1955, she has served as chief of the Section on Bacterial Toxins in the Division of Biologic Standards.

BUREAU OF STANDARDS

Supplement to Radiation Handbooks.—An 8-page supplement to the National Bureau of Standards Handbooks dealing with radiation protection and related matters has been prepared by the National Committee on Radiation Protection and Measurements (NCRP). It is entitled "Maximum Permissible Radiation Exposures for Man" and summarizes the new recommendations of the NCRP on safe limits of radiation exposure. It extends and clarifies "Maximum Permissible Radiation Exposures to Man" (*NBS Tech. News Bull.* 41:17 [Feb.] 1957) but is in general conformity with the philosophy expressed in "Report on 1956 Amendments to the Recommendations of the International Commission on Radiological Protection (ICRP)" (*Radiology* 70:261 [Feb.] 1958). The recommendations of the NCRP are regularly published in the National Bureau of Standards handbook series. Several of these handbooks are being revised to bring them into conformity with the new recommendations. Pending the availability of the revised handbooks, the present supplement provides a simplified statement of the changes needed to comply with the new recommendations.

DEATHS

Antine, William Ⓜ Brooklyn; Long Island College Hospital, Brooklyn, 1926; specialist certified by the American Board of Internal Medicine; member of the American College of Gastroenterology; associated with the Israel-Zion, Maimonides, and Coney Island hospitals; died June 24, aged 54, of coronary thrombosis.

Bailey, Neil Herbert Ⓜ Hartford, Conn.; College of Physicians and Surgeons, Baltimore, 1911; at one time deputy health officer for the city of Hartford; associated with St. Agnes Home in West Hartford, St. Francis and McCook Memorial hospitals; consulting obstetrician to Manchester (Conn.) Memorial Hospital and the Rockville City Hospital in Rockville; died in St. Francis Hospital June 30, aged 78.

Bailey, Robert Ⓜ Coleman, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1906; veteran of World War I; on the staff of Overall Memorial Hospital, where he died July 4, aged 76, of paralysis agitans.

Baltz, James Ian Ⓜ Detroit; State University of Iowa College of Medicine, Iowa City, 1927; fellow of the American College of Physicians; on the staff of the Henry Ford Hospital, where he died June 29, aged 61, of abdominal carcinomatosis.

Beck, August Leo, New Rochelle, N. Y.; born in New York City June 25, 1883; University and Bellevue Hospital Medical College, New York City, 1908; specialist certified by the American Board of Otolaryngology; veteran of World War I; an associate member of the American Medical Association; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological Association, and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; formerly assistant professor of ophthalmology at the New York University Post-Graduate Medical School in New York City; for many years associated with the New Rochelle Hospital, where he was at one time president of the medical board, and where he died July 6, aged 75, of pulmonary embolus.

Becker, Charles J. Ⓜ Milwaukee; Marquette University School of Medicine, Milwaukee, 1916; died in St. Joseph's Hospital July 4, aged 75.

Benjamin, Raymond Gordon Ⓜ Nazareth, Pa.; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1943; served an internship at St. Luke's Hospital in New York City and Easton (Pa.) Hospital; veteran of World War II; died July 5, aged 41, of coronary occlusion.

Bennette, Edgar Clark, Richwood, W. Va.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1895; served as mayor of Richwood and postmaster; on the staff of the Sacred Heart Hospital; died June 27, aged 88.

Bernheimer, Leopold Benno Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1922; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and the American College of Allergists; associated with the Veterans Administration Hospital in Hines, and the Cook County Hospital; on the staff of the Michael Reese Hospital, where he died July 15, aged 61, of carcinoma of the rectum and diabetes mellitus.

Black, John Joseph Ⓜ Brooklyn; Fordham University School of Medicine, New York City, 1918; fellow of the International College of Surgeons and the American College of Surgeons; director of surgery at the Rockaway Beach (N. Y.) Hospital and Dispensary; on the staff of St. Catherine's Hospital; consultant at St. Joseph Hospital in Far Rockaway; for many years chairman of the school board in the Greenpoint section of Brooklyn; veteran of World War I; during World War II chairman of the draft board; died July 7, aged 62.

Boodel, John Cullen Ⓜ Chicago; Northwestern University Medical School, Chicago, 1913; fellow of the International College of Surgeons; associated with Cook County and Evangelical hospitals; died in Toledo, Ohio, July 8, aged 67, of a heart attack.

Boyd, Tullie Van, East St. Louis, Ill.; St. Louis University School of Medicine, 1910; veteran of World War I; died July 10, aged 76, of coronary heart disease.

Brenckle, Jacob Frederick, Superior, Wis.; Milwaukee Medical College, 1897; an associate member of the American Medical Association; veteran

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Ⓜ Indicates Member of the American Medical Association.

of World War I; associated with the Community Memorial Hospital in Redfield, S. D.; died June 26, aged 82, of coronary occlusion.

Buka, Robert Jr., Boston; University of Pittsburgh School of Medicine, 1942; member of the Massachusetts Medical Society; specialist certified by the American Board of Internal Medicine; served on the faculty of Harvard Medical School; veteran of World War II; associated with the Beth Israel Hospital; medical director of the Recuperative Center of the Jewish Women's Health Association; burned to death June 26, aged 40, when his home caught fire.

Calandriello, John J. Ⓜ Brooklyn; Fordham University School of Medicine, New York City, 1917; member of the American Academy of General Practice; veteran of World War I; died in the Brooklyn Hospital June 5, aged 67, of uremia, nephrosclerosis, and diabetes mellitus.

Calhoun, George Arthur, Clairton, Pa.; Baltimore Medical College, 1909; for many years school physician; an associate member of the American Medical Association; died in Harrisburg June 18, aged 74.

Campbell, Theodore Ambrose, Wapakoneta, Ohio; Medical College of Ohio, Cincinnati, 1897; veteran of World War I; associated with St. Rita's and Memorial hospitals in Lima; died July 7, aged 83, of coronary thrombosis.

Cannaday, John E., Charleston, W. Va.; born in Floyd, Va., March 17, 1873; University College of Medicine, Richmond, Va., 1901; an associate member of the American Medical Association and in 1907 member of the House of Delegates; member of the founders group of the American Board of Surgery; member of the Southern Surgical Association and the American Association for the Surgery of Trauma; past-president of the Chesapeake and Ohio Railway Surgeons Association; fellow of the International College of Surgeons and the American College of Surgeons; veteran of World War I; associated with the Charleston General Hospital, where he was first visiting surgeon and since 1924 chief of staff, medical director, and president; died June 29, aged 85, of cerebral arteriosclerosis.

Carrell, Frederick Augustus, St. Paul; University of Minnesota College of Homeopathic Medicine and Surgery, Minneapolis, 1890; died in the Ancker Hospital June 29, aged 99, of cardiorespiratory failure and bronchopneumonia.

Cheng, Ensang Waniella, Boston (licensed in Massachusetts in 1909); died in June, aged 80.

Cottrell, Wilson Philip Ⓜ Reeds Spring, Mo.; University of Arkansas School of Medicine, Little Rock, 1908; died July 3, aged 78, of a heart attack.

Cummins, William Walter Jr. Ⓜ Kansas City, Mo.; University of Kansas School of Medicine, Kansas City, Kan., 1936; veteran of World War II; died in the Research Hospital June 27, aged 47, of cerebral hemorrhage.

Cutler, Condict Walker Jr. Ⓜ New York City; born in Morristown, N. J., Aug. 9, 1888; Columbia University College of Physicians and Surgeons, New York City, 1912; served on the faculty and at one time an alumni trustee at his alma mater; past-president of the Columbia College Alumni Association; veteran of World War I; in 1940 was appointed by Mayor La Guardia a member of an official Advisory Health Preparedness Committee; served during World War II and was awarded the Legion of Merit, a Presidential Citation, and the Congressional Medal for meritorious service; specialist certified by the American Board of Surgery; member of the American Surgical Association, International Society of Surgeons, and American Society for Surgery of the Hand; fellow of the American College of Surgeons; author of "The Hand: Its Disabilities and Diseases"; formerly director of surgery at the Goldwater Memorial Hospital in Welfare Island, where he was a consultant; consultant, Morristown (N. J.) Hospital, and Rockland State Hospital in Orangeburg, N. J.; for many years associated with the Roosevelt Hospital, where he died July 6, aged 69.

Dehli, Herbert Marthinus Ⓜ Colton, S. D.; State University of Iowa College of Medicine, Iowa City, 1932; member of the American Academy of General Practice; president of the school board; associated with the McKennan and Sioux Valley hospitals in Sioux Falls; died June 25, aged 53, of injuries received in an automobile accident.

del Villar, Euripedes Jose, St. Joseph, Mo.; Universidad de Santo Domingo Facultad de Medicina, Dominican Republic, 1948; served an internship at the Riverside Sanitarium and Hospital in Nashville, Tenn., and the Provident Hospital in Chicago; formerly a resident in obstetrics and gynecology at the Kansas City General Hospital in Kansas City, Mo.; died June 6, aged 35, of poison, self-administered.

Dutcher, William Austin, North Berwick, Maine; Tufts College Medical School, Boston, 1905; died May 21, aged 86, of arteriosclerotic cardiovascular disease.

Eckwall, Hubert John, Chicago; Bennett Medical College, Chicago, 1914; veteran of World War I; died in the Alexian Brothers Hospital July 9, aged 70, of pulmonary edema and myocardial degeneration.

Elliott, Hoffman Tyrell Ⓜ Logan, W. Va.; Howard University College of Medicine, Washington, D. C., 1932; member of the advisory committee to the Logan County Board of Education; superintendent of the Denmar (W. Va.) Sanatorium; died in the Pocahontas Memorial Hospital, Marlinton, June 23, aged 57, of ruptured aortic aneurysm.

Engel, Samuel Ⓜ San Francisco; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1922; specialist certified by the American Board of Ophthalmology; member of the Association for Research in Ophthalmology; clinical instructor in surgery (ophthalmology) at Stanford University School of Medicine; associated with Stanford University Hospital; died June 28, aged 59, of cancer.

Enns, Jacob Harlow Ⓜ Newton, Kan.; Rush Medical College, Chicago, 1911; died June 26, aged 76.

Fein, Louis Ⓜ Springfield, Mass.; Tufts College Medical School, Boston, 1929; member of the American Academy of General Practice; on the staff of the Springfield Hospital; died June 26, aged 54, of coronary infarct.

Frishman, Morris, Pittsburgh; Johns Hopkins University School of Medicine, Baltimore, 1917; an associate member of the American Medical Association; member of the American Trudeau Society; died in Mercy Hospital April 26, aged 67, of intestinal obstruction.

Gale, Ailie May Spencer, Bakersfield, Calif.; Cooper Medical College, San Francisco, 1905; for many years a medical missionary in China; died March 27, aged 79, of cancer.

Goodwin, Anna Helena, Bala Cynwyd, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1889; formerly on the staff of the West Philadelphia Hospital for Women in Philadelphia; died June 26, aged 96.

Gorsline, Clarence Samuel Ⓜ Battle Creek, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1901; specialist certified by the American Board of Radiology; member of the House of Delegates of the American Medical Association from 1925 to 1936; member of the American Roentgen Ray Society; past-president and secretary of the Calhoun County Medical Society; served as president of the Michigan Association of Industrial Physicians and Surgeons; on the staffs of the Leila Y. Post Montgomery Hospital and the Community Hospital, where he died June 20, aged 82, of cerebral thrombosis.

Greenwald, Theodore Lawrance Ⓜ Morristown, N. J.; Hahnemann Medical College and Hospital of Philadelphia, 1933; associated with Orange (N. J.) Memorial Hospital and All Souls Hospital; died June 26, aged 50, of coronary thrombosis.

Guarino, Francis Louis, Woodhaven, N. Y.; Long Island College Hospital, Brooklyn, 1907; an associate member of the American Medical Association; died in the Mary Immaculate Hospital, New York City, May 26, aged 74, of bronchopneumonia, diabetes mellitus, and arteriosclerotic heart disease.

Hertzberg, David Ⓜ New York City; Long Island College Hospital, Brooklyn, 1917; service member of the American Medical Association; died in the Fordham Hospital June 3, aged 74, of coronary thrombosis and arteriosclerosis.

Hill, Edward Curtis Ⓜ Denver; Gross Medical College, Denver, 1891; served on the staff of St. Anthony's Hospital; died May 2, aged 94, of arteriosclerotic heart disease.

Hill, Prescott Tillinghast Ⓜ Providence, R. I.; Harvard Medical School, Boston, 1911; member of the American Trudeau Society; served on the staffs of the Charles V. Chapin Hospital and the Rhode Island Hospital, where he died June 26, aged 72, following removal of substernal thyroid.

Hodgins, Thomas Earl Jr. Ⓜ Jacksonville, Fla.; Vanderbilt University School of Medicine, Nashville, Tenn., 1951; connection with the U. S. Public Health Service terminated Oct. 4, 1955; associated with St. Luke's Hospital, Duval Medical Center, and St. Vincent's Hospital; died June 22, aged 32, of a heart attack.

Jacoby, Hans Ⓜ Huron, S. D.; Schlesische-Friedrich-Wilhelms-Universität Medizinische Fakultät, Breslau, Prussia, 1926; associated with the St. John's Hospital; died May 15, aged 56, of cerebral hemorrhage.

King, Lowell Waldo Ⓜ Salem, Ohio; Western Reserve University School of Medicine, Cleveland, 1918; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; on the staffs of the Central Clinic and Hospital and the Salem City Hospital; died in Youngstown June 29, aged 66, of injuries received in an automobile accident.

Kroner, Jacques, New York City; Julius-Maximilians-Universität Medizinische Fakultät, Würzburg, Bavaria, Germany, 1925; member of the Medical Society of the State of New York; died June 19, aged 57, of occlusive coronary arteriosclerosis.

Kurschner, David Milton Ⓜ Shenorock, N. Y.; University of Illinois College of Medicine, Chicago, 1932; specialist certified by the American Board of Internal Medicine; associated with Lebanon Hospital and on the staff of the Home and Hospital of the Daughters of Jacob, New York City; died in the Northern Westchester Hospital in Mount Kisco April 26, aged 54, of acute pulmonary edema.

Larsen, Antonius Andrew Ⓜ South Sioux City, Neb.; University of Nebraska College of Medicine, Omaha, 1918; member of the American Academy of General Practice; died June 26, aged 66.

Lennard, Oswald Dawkins, Verplanck, N. Y.; Meharry Medical College, Nashville, Tenn., 1928; member of the Medical Society of the State of New York; on the staff of the Harlem Hospital, New York City, where he died June 30, aged 64.

Lovvorn, Robert M., Richland, Ga.; University of Georgia Medical Department, Augusta, 1889; also a Baptist minister; died in Bowdon June 22, aged 92.

McClernan, Bertha K. Mackel, Butte, Mont.; University of Minnesota College of Medicine and Surgery, Minneapolis, 1899; died June 1, aged 84.

McCooey, James Henry Ⓜ Woonsocket, R. I.; College of Physicians and Surgeons, Baltimore, 1906; died June 29, aged 74, of myocardial insufficiency.

McCoy, Bernice Ⓜ Whittier, Calif.; University of Pennsylvania School of Medicine, Philadelphia, 1924; veteran of World War II; served with the maternal and child hygiene division of the Los Angeles County Health Department; died June 13, aged 62, of dissecting aneurysm of the aorta and arteriosclerosis.

Maclaire, Aaron Scott, New York City; Columbia University College of Physicians and Surgeons, New York City, 1918; died June 8, aged 63, of coronary arteriosclerosis and fibrosis of the left ventricle.

Mansfield, Thomas Richard, Framingham, Mass.; Boston University School of Medicine, 1929; served on the faculty of his alma mater; veteran of World War II; died in the Leonard Morse Hospital, Natick, June 28, aged 57, of coronary occlusion, myocardial infarction, and ruptured left ventricle.

Manss, Charles Walter, Cincinnati; Miami Medical College, Cincinnati, 1902; died in Arlington, Va., June 28, aged 81.

Merkatz, Harry, New York City; University and Bellevue Hospital Medical College, New York City, 1928; died in the New York Hospital May 2, aged 56, of cerebrovascular accident and cerebrovascular arteriosclerosis.

Meyer, Julius Felix Ⓜ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1910; served on the staffs of the Children's Memorial, Michael Reese, and Edgewater hospitals; died July 3, aged 78, of heart disease.

Nelson, Anton N., Clear Lake, Wis.; Milwaukee Medical College, 1907; president of the Bank of Clear Lake; died in La Crosse June 25, aged 80, of coronary disease.

Patterson, John Gordon, Klamath Falls, Ore.; Willamette University Medical Department, Salem, 1903; Jefferson Medical College of Philadelphia, 1908; past-president of the Klamath County Medical Society; died in the Hillside Hospital June 23, aged 86.

Preston, John Bruno Ⓜ Chicago; University of Illinois College of Medicine, Chicago, 1943; also a graduate in pharmacy; veteran of World War II; interned at the Cook County Hospital; specialist certified by the American Board of Surgery; served a residency at the Veterans Administration Hospital in Oklahoma City, Okla., and St. Mary of Nazareth Hospital, where he was a member of the staff, and where he died July 3, aged 41, of generalized metastatic carcinoma and testicular seminoma.

Probst, Everett William Ⓜ Rutherford, N. J.; University and Bellevue Hospital Medical College, New York City, 1930; member of the American Academy of General Practice, American Academy of Occupational Medicine, and the Industrial Medical Association; veteran of World War II; medical director of Reaction Motors Inc., Denville; associated with the Riverside Hospital in Boonton and the Dover (N. J.) General Hospital, where he died May 22, aged 53, of myocardial infarction.

Rooney, Paul Neill Anthony, Boston; Harvard Medical School, Boston, 1924; member of the Massachusetts Medical Society; awarded the Distinguished Service Cross during World War I; associated with Faulkner Hospital and St. Elizabeth's Hospital, where he died June 16, aged 63, of acute focal pericholangitis and choledocholithiasis.

of directors of Seaside Memorial Hospital; on the staffs of St. Mary's and Community hospitals; died in Banning June 29, aged 58, of cancer of the lung.

Ward, Sherman Carl, Lorain, Ohio; University of Michigan Medical School, Ann Arbor, 1915; member of the Ohio State Medical Association; served as county coroner; on the staff of St. Joseph's Hospital, where he died June 29, aged 66, of coronary occlusion and arteriosclerotic heart disease.

Warren, George Hilliard, Perry, Fla.; St. Louis University School of Medicine, 1904; died May 30, aged 81, of cerebrovascular accident and generalized arteriosclerosis.

Weber, William Lewis, Philadelphia; Medico-Chirurgical College of Philadelphia, 1914; an associate member of the American Medical Association; served on the city department of health; since 1925 on the staff of the Abington (Pa.) Memorial Hospital; died in the Graduate Hospital of the University of Pennsylvania June 18, aged 68, of dissecting aneurysm.

Weinberg, Frederick Samuel, New York City; Universität Heidelberg Medizinische Fakultät, Baden, Germany, 1911; died May 30, aged 69, of congestive heart failure and generalized arteriosclerosis.

White, Edward Olin Ⓜ Madison, Ga.; Medical College of South Carolina, Charleston, 1946; member of the American Academy of General Practice; on the staff of St. Mary's Hospital in Athens; died June 18, aged 35, of coronary occlusion.

White, John Keller, Sayville, N. Y.; Long Island College of Medicine, Brooklyn, 1946; member of the Medical Society of the State of New York; interned at the Brooklyn Hospital; certified by the National Board of Medical Examiners; a captain in the medical corps, Army of the United States; served on the staff of the Little Falls (N. Y.) Hospital; killed in a plane crash June 29, aged 37.

Wiener, Isidore Kalisch Ⓜ Watervliet, N. Y.; Johns Hopkins University School of Medicine, 1911; specialist certified by the American Board of Otolaryngology; formerly on the faculty of the University and Bellevue Hospital Medical College in New York City, where he was associated with the Mount Sinai Hospital, Hospital for Joint Diseases, and Harlem Hospital; industrial physician at the Watervliet Arsenal; died in the Albany (N. Y.) Hospital June 18, aged 74, of cancer.

Williams, Benjamin Franklin, Salem, Ore.; Lincoln (Neb.) Medical College of Cotner University, 1899; specialist certified by the American Board of Psychiatry and Neurology; fellow of the American Psychiatric Association; veteran of World War I; for many years superintendent of the Nebraska Hospital for the Insane in Lincoln, Neb.; served as chairman of the board of control for state institutions in Nebraska; associated with the Oregon State Hospital; died June 23, aged 82, of cerebral hemorrhage.

Williams, Nathan Bangs Ⓜ Belle Plaine, Iowa; State University of Iowa College of Medicine, Iowa City, 1927; president of the city park board; served as a member of the board of education and as director of the Citizens State Bank; associated with Mercy Hospital and St. Luke's Hospital in Cedar Rapids, where he died June 24, aged 57, of pulmonary embolus.

Wills, Thomas Edmund Ⓜ Pottstown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; served on the staff of the Pottstown Hospital; died June 4, aged 87, of pulmonary embolism.

Wilson, Talmadge S. Ⓜ Lieut. Commander, U. S. Navy, retired, Stuart, Fla.; University of Georgia Medical Department, Augusta, 1914; retired from the Navy on June 30, 1937; veteran of World Wars I and II; for many years practiced in Paterson, N. J., where he was on the staff of the Paterson General Hospital; service member of the American Medical Association; associated with the Martin County Hospital; died June 15, aged 68, of a heart attack.

Winston, Joseph Pendleton, Anchorage, Ky.; University of Virginia Department of Medicine, Charlottesville, 1892; an associate member of the American Medical Association; died in the Pewee Valley (Ky.) Sanitarium and Hospital June 15, aged 88.

Wolfe, Clinton Silvester, Topeka, Kan.; Bennett Medical College, Chicago, 1909; died June 17, aged 75.

Writt, William Morgan Ⓜ Sharon, Pa.; University of Pittsburgh School of Medicine, 1911; associated with the Sharon General Hospital; died June 10, aged 69, of a heart attack.

Zinsser, Harry Frederick, Pittsburgh; University of Pennsylvania School of Medicine, Philadelphia, 1912; an associate member of the American Medical Association; clinical professor of medicine at the University of Pittsburgh School of Medicine; associated with Presbyterian Hospital and St. Francis Hospital, where he was staff president and where he died June 22, aged 71, of carcinoma of the colon with metastases.

FOREIGN LETTERS

AUSTRIA

Changes in the Veins Following Injuries.—At the meeting of the Society of Physicians in Vienna on June 27, Drs. R. Gottlob and G. Zinner said that the technique developed by O'Neill to demonstrate endothelial cells by silver impregnation of the interstitial substance had been modified in such a way that it could be used on the venules of a rabbit. The lesions caused by various injuries were classified as follows: O, normal intima and regular cell boundaries; I, thornapple shape of the intima; II, partial destruction of the interstitial substance and interrupted cell boundaries; III, cell boundaries no longer recognizable and staining of the deeper layers by the silver nitrate solution. The above mentioned lesions develop after mechanical injuries, chemical injuries, or surgical intervention near the veins. After irradiation with x-rays lesions were observed at the time of the early erythema and then again about 10 weeks later. In the presence of lesions of groups II and III the permeability was always greatly impaired. This could be easily demonstrated by applying Evans-blue solution. In normal and slightly damaged areas the stain could not penetrate into deeper layers but in more severe injuries the stain penetrated into the deeper layers and could not be removed by washing the vein. After the intima had been treated with histamine, no morphological lesions nor any disturbance of permeability could be demonstrated by means of the above described method. This finding supports the belief that histamine does not in the first instance impair permeability but acts only secondarily to impair permeability following a disturbance of the precapillary circulation.

Endothelial Lesions Due to Contrast Mediums.—At the same meeting the same doctors stated that local lesions produced by radiopaque contrast mediums might occur in the walls of blood vessels in the kidneys or central nervous system, particularly in the vascular endothelium. Impairment of the vascular wall after such exposure was not revealed by the histological stains in general use but only after staining of the interstitial substance with 0.25% silver nitrate solution. In this way severe impairment of the endothelium could be demonstrated following the action of the commonly used iodized contrast mediums. Simultaneous tests were made with glucose solution of the same percentage and under the same conditions. Neither glucose nor contrast medium caused endothelial damage in a 5% solution but promptly produced maximal endothelial damage in a 15% solution. These stronger concentrations simultaneously produced severe disturbance of permeability, manifested by diffusion of a stain like Evans-blue through the impaired endothelium, whereas the 5% solution produced no disturbance of permeability. A phlebogram of a rabbit showed that impairments by contrast mediums occur especially in the area of the valves of the veins. The speakers stressed the powerful effect such mediums have on the vascular endothelium and the disturbance of permeability and thrombus formation resulting therefrom.

Acceleration of Parturition.—At the meeting of the Austrian Society of Obstetrics and Gynecology in Graz in May, Dr. E. Leinzinger stated that a marked acceleration of delivery can be effected by the administration of Lyspamin (1-nicotinylamino-1, 2-diphenylethane) combined with Hydergine (a mixture of hydrogenated ergot alkaloids). Dilatation of the cervix was accelerated as compared to the untreated controls. Methylergonovine therapy, which also reduces the loss of blood in addition to the acceleration of this stage, is recommended in the third phase of labor.

CANADA

Mammary Artery Implantation for Coronary Disease.—A. Vineberg (*Canad. M. A. J.* 78:871, 1958) based his concept of the myocardial circulation in health and disease on certain anatomic and pathological facts that are frequently ignored. He noted that the extensive arteriolar network in the myocardium received arterial blood directly from the coronary arteries and was usually free from disease even when its supplying coronary arteries were sclerotic. Burying an internal mammary artery in the myocardial tunnel made in the left ventricle brings an extracardiac source of blood to the myocardium, and a connection is made between the buried artery and the coronary circulation. Vineberg described his own method of producing gradual coronary occlusion in dogs and noted that when internal mammary artery implantations were performed on these animals, exercise or excitement more than five months later did not produce death, as it did in controls. Autopsy showed that 89% of the implanted arteries were patent and 84% had formed mammary-coronary anastomoses. The following criteria for performing mammary artery implantation in patients was suggested. They should have proved coronary artery disease with

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The items in these letters are contributed by regular correspondents in the various foreign countries.

typical angina pectoris and at least one to two years of adequate medical treatment. The operation should not be performed when the patient is symptom-free, when there is evidence of disease activity or of left ventricular failure, or when the patient has angina at rest. The operative mortality for patients with no angina at rest is 5%, whereas with angina decubitus it is 59%. Late mortality is similarly related to the degree of angina. Six months to seven years after operation, 30 patients (75% of the original group) were still alive and 24 were working full time.

Tetanus Neonatorum.—According to a report in the *Canadian Medical Association Journal* (78:922, 1958) six cases of tetanus neonatorum occurred in a rural negro community in four years. In this community, normal birth takes place at home under the direction of a handy woman who usually looks after animals. These women have no formal training and treat the umbilical cord with daily dressings of soft paraffin dug from the container by finger and applied on gauze. In all but one of the cases listed death took place in spite of standard treatment with tetanus antitoxin, and in all but one common pathogenic bacteria were cultured from the umbilicus. It was difficult to decide on a dose of sedative that would adequately control tetanic spasms without dangerously depressing respiration. Antitoxin appeared to be useless.

Federation of Biological Societies.—Last year, the Canadian Physiological Society, the Pharmacological Society of Canada, the Canadian Association of Anatomists, and the Canadian Biochemical Society joined forces to form a Canadian Federation of Biological Societies. The first joint annual meeting of these societies was held in Kingston, Ontario, in June. Dr. R. Altschul of the University of Saskatchewan reported that nicotinamide is of no use in lowering the serum cholesterol level but that sodium nicotinate, much better tolerated than nicotinic acid, has this effect in short-term experiments. Long-term administration to patients will be the next investigational step. Beaton of the University of Toronto stated that anterior pituitary growth hormone has a direct effect on fat metabolism and that this effect may be interrelated with changes in protein metabolism. Acute pancreatitis is perpetuated by tryptic and lipasic autolytic processes. Beck and co-workers, of Montreal, have been searching for compounds which would inhibit this autolysis and might therefore be of therapeutic value in acute pancreatitis. They found that Hyamine 1622 (p-diisobutyl phenoxy ethoxy dimethyl benzyl ammonium chloride) diminishes the proteolytic activity of trypsin but does not inhibit chymotrypsin, pepsin, or lipase. Beveridge of Kingston, Ontario, produced evidence suggesting that the substance in corn oil responsible for lowering blood cholesterol levels was in the unsaponifiable matter and not in the unsaturated fatty acids. Brouillet of Montreal showed that there was no significant change in urinary aldosterone or 17-hydroxycorticosteroid excretion in patients given infusions of epinephrine or levarterenol.

Campbell and Chapman of the Food and Drug Laboratories in Ottawa have developed a method of rating foods which might be used as a basis for judging the validity of advertising claims. They propose a protein rating based on both quality and quantity of protein in the food. The food is fed as a sole source of protein at a level of 10% and a protein efficiency factor determined from the effect of the food on rat growth. The protein rating is obtained by multiplying the protein efficiency ratio by the weight of protein in a reasonable daily intake of food. A food with the rating of 40 or greater may be referred to as an "excellent dietary source of protein" and one with a rating of 20 to 39 as a "good dietary source of protein."

Hawkins of Halifax showed that alpha-tocopherol phosphate had an anticoagulant effect on the blood of dogs and rabbits and also an antilipemic effect. Kumar noted a tendency to high aldosterone excretion and low intracellular sodium values in normal pregnancy, with a tendency to high intracellular sodium and lower aldosterone values in preeclampsia. Lenoski of Manitoba induced hypocapnia by passive hyperventilation in flying personnel and showed that those persons whose performance was impaired during hypocapnia benefited significantly by administration of acetazolamide. Mazurkiewicz stated that chlorpromazine is capable of reducing the analgesic dose of morphine but does not retard development of tolerance to the latter. McCarter of Dalhousie University found that a single application of a carcinogenic hydrocarbon in a volatile solvent to the skin of a mouse could produce an effect that was virtually maximal when the period of exposure was less than one hour.

Raeside of Montreal found that the urinary estrogen was diminished in most but not all pregnant diabetic women and that when values were low this was associated with intrauterine death of the fetus. Rona of Montreal reported that rabbits given cholesterol dissolved in unsaturated fatty acids had a significantly higher cholesterol level and more marked atherosclerosis than rabbits given cholesterol dissolved in olive oil. Marc-Aurèle of Montreal studied two new diuretic agents, chlorothiazide and spirolactone. Spirolactone in oral doses of 150 mg. every four or six hours produced significant sodium diuresis with transient lowering of urinary potassium in patients with generalized edema. No side-effects were noted.

Bone-Marrow Homotransplantation for Leukemia.—Reports of work in which mice previously treated by intravenous injection of homologous bone marrow withstood whole body irradiation in doses approximating the 100% lethal dose, given for mouse leukemia, have raised hopes that a similar form of treatment might be applied successfully in patients with leukemia. It would seem that the marrow of the irradiated animal is destroyed and the injected hematopoietic material repopulates the recipient's marrow sites. Meighan and Bean (*Canad. M. A. J.* 78:858, 1958) attempted this form of therapy in a patient whose chronic lymphoid leukemia had withstood all other forms of treatment. They obtained marrow aspirations from the patient's sister and administered the aspirate to the patient through the saphenous vein, introducing a 0.01-mm. steel wire mesh screen between the syringe and the cannula. On the day before this was done, the patient was given 700 r whole body radiation, with a treatment time of six hours. The total number of nucleated cells injected into the patient was about 4 billion. Death ensued five days later. In spite of the large dose of radiation given, primitive immature cells were still present in the patient's peripheral circulation, and the marrow still contained abundant lymphocytic material at the time of death. Despite a careful search, no evidence of a marrow take was found. In this case there may have been host rejection of the donor marrow, the dose of whole body radiation may have been too great or too small, and the amount of bone marrow injected may have been insufficient. There may have been a failure of donor marrow to pass the lung barrier, or the patient's general condition may have been so poor that he was unable to tolerate the procedure. In future application of this technique, an attempt should be made to remove the fat from the bone marrow.

Too Many Doctors in Canada?—A note in the *Canadian Medical Association Journal* for June 15 discussed two conflicting statements recently made about the present and projected needs for physicians in Canada. The Dominion Council of Health indicated a need for more physicians, while Dr. R. Struthers, a noted physician in academic and research fields, stated that apparently needs are being adequately met and that it is time to call a halt to the extension of Canadian medical schools. The present analysis pointed out the variable factors that should be taken into account. Thus, for example, the demand for services is in many ways directly related to population growth and age distribution. It appears that by 1975 Canadian requirements for physicians, if the present population-physician ratio is to be maintained, will be 54% greater than in 1955. The fact that this ratio has remained constant for so long is surprising in view of the many factors affecting it. The developing insurance mechanisms in Canada will certainly increase the existing demand and create a new demand for physicians. Furthermore as the income in Canada increases the public will be willing to appropriate a greater proportion of its income for medical services. The analyst suggested an increase in demand approximating 2.5% per year in the near future, rising to 3% per year on a long-term basis. This will mean a net increase of 400 new physicians each year. Another factor affecting calculations is retirement age. Data from the new Canadian Medical Retirement Savings Plan suggest that many physicians are now planning to retire at ages 55, 60, or at the latest 65. The present retirement age averages 71 years. The analysis suggested a near future requirement for new physicians equal to 6% of the present physician population, rising in 15 to 20 years to 7%. Demands are being met not by Canadian medical schools but by an unprecedented rate of immigration. The present situation would suggest that a figure of 500 immigrant physicians each year will be needed to make up the deficit.

Retirement Savings Plan.—The Canadian Medical Retirement Savings Plan, sponsored and administered by the Canadian Medical Association, is in a healthy state. Total contributions from physicians to date amount to over 2 million dollars; 38% of this went at the desire of the contributors into the insured annuity fund and 62% into the common stock fund. The basic outlines of the plan are simple and flexible. Participation enables a physician to obtain tax relief now on the savings he invests to provide retirement income. The physician may specify his percentage allocation to the common stock fund, chosen by a trusteeship committee which has a nucleus in Toronto and corresponding members in the provinces and has spread its stock purchases over a wide range including banks, distilleries and breweries, building products, chain stores, aluminum, glass, paper, power, and telephone companies, oil, and insurance. On the other hand the physician may elect to put most of his savings into an insured annuity fund, where there is a guaranteed rate of 3.5% per annum, presently being exceeded.

INDIA

Intracardiac Operations at Normal Temperature.—Pritam Das (*Journal of the Indian Medical Association*, vol. 30, June 16, 1958) reported a study on dogs which was undertaken to assess the possibility of intracardiac operations under direct vision at normal temperature. It was found that the heart could not tolerate occlusion of the superior and inferior venae cavae and the vena azygos for more than three to five minutes. If, however, blood was allowed to flow through the azygos vein while the two venae cavae were occluded, the right atrium could then be opened widely without loss of blood. The blood from this chamber was sucked out completely and the various landmarks visualized. Intracardiac operations were therefore tried under these circumstances, when the two venae cavae were occluded for 10 to 15 minutes; 17 operations were performed on dogs, in 14 of which the right atrium was explored, while in 3 the right ventricle was opened and the orifice of the pulmonary trunk dilated. Changes in the pulse, blood pressure, and electrocardiogram were recorded and the safety of the procedure assessed. The right atrium could never be made completely dry because of blood flow from the azygos vein and the coronary sinus but such landmarks as the atrioventricular orifice, fossa ovalis, and orifices of the superior and inferior venae cavae could be visualized.

The occlusion of the superior vena cava alone did not affect the rate or rhythm of the heart. But as soon as the inferior vena cava was occluded marked changes were seen. The heart rate became slow, sometimes following an initial quickening. In only one case it did not become slow, while in two others it remained a little quicker than the initial rate during the whole period of occlusion. The release of veins caused a sudden rise almost to the normal level. Irregularities of rhythm appeared when stray sutures were passed in the wall of the atrium or when the finger was placed in the tricuspid ring and orifice of the superior vena ca On release of the inferior vena cava, there distention of the atrium and ventricle, and i larities such as extrasystole and missing of appeared. In all cases the heart was mod distended and blue. In six it was overdisten and blue, leading to ballooning of the heart.

The period immediately after release of the inferior vena cava was the most dangerous due to production of overdistention of the chambers. Ventricular fibrillation was not a frequent occurrence in this procedure. Auricular fibrillation was more common but resolved itself spontaneously. No significant changes were observed in the electrocardiogram during the period of occlusion. The blood pressure showed a gradual fall when the superior vena cava was occluded, while occlusion of the inferior vena cava led to a sudden and marked fall in blood pressure. It was maintained at a low level during the period of occlusion and showed little change when the superior vena cava was released, but with release of the inferior vena cava it showed a sudden rise and reached a level higher than the initial. To prevent air embolism, the atrial incision was sutured from below upward, and, while the uppermost part of the incision was still unsutured, the superior vena cava was released, thus filling the atrium with blood which expelled the air through the upper unsutured part of the incision. A small amount of blood was allowed to escape to ensure complete elimination of air.

Of the 17 animals, 5 died on the operating table, 4 of them due to ballooning of the heart; one died two days later with signs suggestive of decerebrate rigidity, but histological examination of the pons and midbrain in this case showed no abnormality; and 11 dogs survived, one of which showed signs of cerebral damage while the others were normal

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was good and convalescence smooth, but if wou
healing was delayed or convalescence not smooth
the level of beta globulin fell. Most patients showed a fall in the total serum proteins in the postoperative period.

Tuberculosis Survey.—A National Pulmonary Tuberculosis Survey was made by the Indian Council of Medical Research. Its main object was to estimate the incidence of pulmonary tuberculosis, to determine from this the extent of the problem, and to devise antituberculosis measures. Previous surveys were so limited in scope that they could not provide a definite picture of the whole country. This survey covered six zones and only those centers that had mass miniature radiography. The sample survey covered in each zone 30 villages, 6 medium-size towns, and 25 to 40 blocks of a city. Villages situated near roads which could be negotiated by heavy mobile x-ray and generator vans were surveyed. Nearly 90% of the population of the zones were x-rayed. Children below 5 years of age were excluded. Field teams consisting of about 20 workers often worked early in the morning and late in the evening as most people were available for examination only at these times. Films of the chest were made by a mass miniature radiography set and a schedule incorporating important and relevant information was filled in for each person. Adequate samples from all zones were examined and compared. Finally six radiologists, including three senior radiologists, gave their independent findings.

It was observed that the bacillary rate per 1,000 persons varied from 1 to 11 in different areas and the number of active and probably active cases from 7 to 30 per 1,000. The morbidity among women was less than that among men. Rates for both men and women showed an increase with age. The rate of increase with age for women was much less than that for men. These were the tentative findings. The results suggested that the incidence of the disease was not diminishing in cities and industrial areas. It had increased in small towns and villages which had previously been comparatively free from tuberculosis and was most marked in villages where it was previously about 0.3%. Here the incidence was approaching that of the cities. Preliminary results indicated that 2% of the country's population was affected by the disease.

The Drug Industry.—A number of steps have been taken by the government to develop the pharmaceutical industry. Existing manufacturers were encouraged to undertake production from intermediates near to basic chemicals. New manufacturers were permitted to enter the field on the basis of their undertaking production of basic drugs as soon as possible in accordance with the programs approved by the government. A proposal for the establishment of a plant to meet the requirements of intermediates, which is under consideration, is expected to be implemented during the Second Five-Year Plan period. Based on expert studies undertaken by suitable agencies, proposals for the establishment of a company for the manufacture of synthetic drugs and additional quantities of antibiotics from basic stages are being considered. There has been a notable increase in the production of penicillin, isoniazid, PAS, and other synthetic drugs. Licenses have also been given for the production of such essential products as vitamin A and cortisone. The production of penicillin in 1957 was more than 1.5 times as great as in 1956, that of isoniazid was more than 3 times, and that of PAS over 10 times as great. The amount of antidysentery drugs produced in 1957 was more than double that of the previous year. The production of insecticides and sulfonamides also increased. The Development Council for Pharmaceuticals and Drugs was reconstituted early in 1957. The council's main functions are to suggest norms of efficiency, secure fuller use of installed capacity, obtain maximum production, improve quality, and promote better marketing facilities. The council also recommends targets of production and coordinates production programs.

Cerebral Infarction.—P. L. Deshmukh (*Journal of the Indian Medical Association*, vol. 30, June 1, 1958) stated that the precipitating factor in the production of coma following cerebral infarction is the extensive edema and the resulting ischemia of the brain in the affected area. Attempts have been made to improve the cerebral circulation in this region by using vasodilators such as tolazoline, aminophylline, nicotinic acid, papaverine, and by blocking the stellate ganglion. The author did not get good results with vasodilators. Results with stellate ganglion block though encouraging were not impressive. Cortisone was then tried on four patients with cerebral infarction. The age of these patients varied between 52 to 74 years. Treatment with cortisone was started 48 hours after coma had set in and was by then fairly deep. Supportive treatment, such as feeding with a nasal tube and attention to bowels and bladder, was maintained during treatment with cortisone. The drug was given subcutaneously in doses of 100 mg. three times a day for the first three days. The dose was then reduced to 100 mg. twice a day for the next two days, 50 mg. twice a day for three days, and 25 mg. twice a day for three days. Later 25 mg. was given twice a day by mouth for about a fortnight. A low salt regimen was observed during this period and 1 to 2 Gm. of potassium chloride per day was given by mouth. A dramatic improvement was seen in 24 hours after commencement of treatment. Consciousness returned gradually and speech showed signs of returning after three days. There was a general sense of well-being. There was reduction of pain in the affected extremities on passive movement and improvement in the range of motion was noticed. The beneficial effect of cortisone in this condition is believed to be due to its antiexudative action which helps in controlling cerebral edema and its property of inhibiting mesenchymal tissue reaction which minimizes irreversible neurological damage.

Liver Damage in Malaria.—Ray and Sharma (*Indian Journal of Medical Research*, vol. 46, May, 1958) stated that earlier experiments had shown that in fatal cases of falciparum malaria in man and knowlesi malaria in monkeys, the liver parenchyma showed swelling, fatty changes, and centrilobular necrosis. There was some correlation between the hepatic lesions and the intensity of infection, especially in respect to necrotic changes. The central hepatic veins showed dilatation and sometimes rupture when the necrotic changes were advanced, while the sinusoids were widely dilated and contained areas of packing with enormously swollen

Kupffer cells, pigment, cell debris, and blood elements which would block the free flow of blood from portal to hepatic veins. There was some indirect evidence of a constrictor mechanism in the hepatic veins controlled by stimuli arising in higher nervous centers and transmitted through the sympathetic system. To get further proof of such a mechanism, the effects of knowlesi malaria on the liver of monkeys which were subjected to sympathectomy were observed and the results were compared to those obtained in another group of infected animals not previously subjected to such an operation.

Thus bilateral sympathectomy between the 6th and 12th thoracic levels was performed on 11 monkeys and 1 monkey was subjected to a standard dose of 5×10^6 parasitized cells from donor monkeys infected with Plasmodium knowlesi. Ten other monkeys similarly infected but not operated on served as controls. The course of infection was more or less the same in all monkeys and all of them died in about five days. Liver biopsy specimens taken just before death showed changes in liver parenchyma in the controls and in the monkey subjected to unilateral sympathectomy which were proportional to the intensity of infection and consisted of fatty changes and necrosis restricted to cells around dilated or even ruptured central hepatic veins. In monkeys with bilateral sympathectomy, these necrotic changes were completely absent and the central hepatic veins were mostly normal in appearance and fatty changes were slight or moderate. Thus bilateral sympathectomy was in some way responsible for preventing the necrosis of the hepatic parenchyma. The changes in sinusoids and their packing with cells, pigments, etc. were the same in all monkeys. This suggested that a sphincter mechanism in the hepatic venous tree was probably responsible for the changes in the central hepatic veins which in turn led to the necrotic changes in cells surrounding the vein and this mechanism was controlled by a center perhaps in the hypothalamus transmitting impulses via the sympathetic nerves. The nature of such a stimulus could be anoxemia or possibly a toxin.

Liver Function in Uremia.—H. Singh (*Journal of the Indian Medical Association*, vol. 30, June 16, 1958) subjected 25 patients with uremia to liver function tests with a view to assessing the liver damage, if any, that may be caused by the associated biochemical disturbances. Patients with any past or present history suggestive of liver disease were excluded. The tests used were Van den Bergh's test; estimation of serum bilirubin, total proteins, serum albumin, and serum globulin; thymol turbidity; cephalin cholesterol and other flocculation test; and alkaline phosphatase estimation. The total serum proteins were found to be within normal limits, the serum albumin was subnormal in three and raised in one patient, and the serum globulin was raised in eight patients. The thymol turbidity and flocculation tests were within normal limits. The cephalin cholesterol flocculation test gave abnormal values in two patients. The serum alkaline phosphatase was raised in 11 patients but this may have been due to the renal disease and may not indicate liver dysfunction. The serum bilirubin was less than 1 mg. per 100 ml. in 24 patients.

Primary Hepatic Carcinoma.—M. D. Divekar (*Journal of Postgraduate Medicine*, vol. 4, April, 1958) reviewed 33 autopsy reports of patients dying of primary carcinoma of the liver; 31 of the patients were men and 2 were women. An overwhelming preponderance of men between 41 and 60 years was noticed. Although infantile cirrhosis is common in India, no case of primary carcinoma of the liver in childhood proved at autopsy was reported in this series. Nausea, vomiting, and abdominal pain were the commonest complaints; 67% of the patients had had pain in the right hypochondrium as the initial symptom. Hematemesis occurred in five patients and proved fatal in two. Jaundice varied between a mild icteric tinge to yellow-green. Ascites was detected clinically in only 22 patients. No malignant cells were seen in the ascitic fluid. The amount of the fluid found at autopsy varied between 500 and 3,000 ml. Fourteen patients had fever, in two of whom it was the initial symptom leading to the erroneous diagnosis of an amebic abscess. The liver was palpable in 20 patients, the lump simulating a gastric neoplasm in one. Moderate enlargement of spleen was seen in 13, mental changes in 2, and 14 became drowsy in the terminal stage and died in a coma. At autopsy only 16 cases showed evidence of hepatic cirrhosis. During the period of the study, hepatic cirrhosis was recorded in about 340 autopsies. Almost all the patients were, however, undernourished. Spread of malignancy to local structures such as the stomach, gallbladder, colon, and diaphragm was seen in some patients, the commonest structure to be involved being the diaphragm. Abdominal lymph nodes were invaded by metastases in 22 patients and mediastinal in 3. There was no evidence of distant metastases in 25, but in others metastases in the lungs, skull, vertebrae, urinary bladder, and adrenals were seen. The portal vein was involved in six patients, the splenic vein in two, and the inferior vena cava in three. In addition, four had pulmonary tuberculosis, three had chronic pancreatitis, and one had cholecystitis and cholelithiasis.

Effect of Diet on Serum Cholesterol.—Gopalan and Ramanathan (*Indian Journal of Medical Research*, vol. 46, May, 1958) stated that the level of fat in the diet may influence serum cholesterol concentration to a certain extent and this in turn is concerned in the pathogenesis of coronary arteriosclerosis. The authors studied the effects of ingestion of high levels of different types of fat on serum cholesterol concentration in human volun-